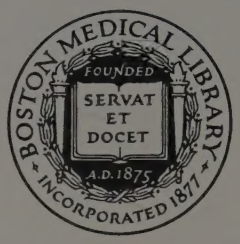
PROLOG

Obstetrics

SEVENTH EDITION

The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

BOSTON
MEDICAL LIBRARY



IN THE
Francis A. Countway
Library of Medicine
BOSTON

Gift of
Cowles Fund

PROLOG

Obstetrics

SEVENTH EDITION

Critique Book

The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

BOSTON MEDICAL LIBRARY
IN THE
FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE

ISBN 978-1-934984-22-2

Copyright 2013 by the American College of Obstetricians and Gynecologists. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, posted on the Internet, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the publisher.

12345/76543

The American College of Obstetricians and Gynecologists
409 12th Street, SW
PO Box 96920
Washington, DC 20090-6920

WQ
18.2
P964
2013
Critique
Book

Contributors

PROLOG Editorial and Advisory Committee

CHAIR

Ronald T. Burkman Jr, MD
Professor of Obstetrics and Gynecology
Tufts University School of Medicine
Division of General Obstetrics and Gynecology
Department of Obstetrics and Gynecology
Baystate Medical Center
Springfield, Massachusetts

MEMBERS

Bernard Gonik, MD
Professor and Fann Srere Chair of Perinatal Medicine
Division of Maternal–Fetal Medicine
Department of Obstetrics and Gynecology
Wayne State University School of Medicine
Detroit, Michigan

Louis Weinstein, MD
Past Paul A. and Eloise B. Bowers Professor and Chair
Department of Obstetrics and Gynecology
Thomas Jefferson University
Philadelphia, Pennsylvania

Linda Van Le, MD
Leonard Palumbo Distinguished Professor
UNC Gynecologic Oncology
University of North Carolina School of Medicine
Chapel Hill, North Carolina

PROLOG Task Force for *Obstetrics*, Seventh Edition

COCHAIRS

Vincenzo Berghella, MD
Director, Division of Maternal–Fetal Medicine
Professor, Department of Obstetrics and Gynecology
Thomas Jefferson University
Philadelphia, Pennsylvania

George A. Macones, MD
Mitchell and Elaine Yanow Professor and Chair
Department of Obstetrics and Gynecology
Washington University in St. Louis
St. Louis, Missouri

MEMBERS

Cynthia Chazotte, MD
Professor of Clinical Obstetrics and Gynecology and Women's Health
Department of Obstetrics and Gynecology
Weiler Hospital of the Albert Einstein College of Medicine
Bronx, New York

Donna D. Johnson, MD
Professor and Chair
Department of Obstetrics and Gynecology
The Medical University of South Carolina
Charleston, South Carolina

Elizabeth G. Livingston, MD
Division of Maternal–Fetal Medicine
Department of Obstetrics and Gynecology
Duke University Medical Center
Durham, North Carolina

Continued on next page

PROLOG Task Force for *Obstetrics*, Seventh Edition
(continued)

Deborah S. Lyon, MD
Department of Obstetrics and Gynecology
Memorial Hospital
Jacksonville, Florida

Keith H. Nelson, MD
Associate Professor, Interim Division Director
Assistant Program Director
Department of Obstetrics and Gynecology
East Carolina University Brody School of Medicine
Greenville, North Carolina

Christian M. Pettker, MD
Medical Director, Labor and Birth Unit
Assistant Professor, Section of Maternal–Fetal Medicine
Department of Obstetrics, Gynecology, and Reproductive Sciences
Yale University School of Medicine
New Haven, Connecticut

Lauren A. Plante, MD, MPH
Associate Professor
Departments of Obstetrics and Gynecology and Anesthesiology
Director, Division of Maternal–Fetal Medicine
Drexel University College of Medicine
Philadelphia, Pennsylvania

Michael P. Plevyak, MD
Assistant Professor of Obstetrics and Gynecology
Division of Maternal–Fetal Medicine
Associate Program Director, Obstetrics–Gynecology Residency
Tufts University School of Medicine
Baystate Maternal–Fetal Medicine
Springfield, Massachusetts

John M. Thorp Jr, MD
Hugh A. McAllister Distinguished Professor
Department of Obstetrics and Gynecology
University of North Carolina
Chapel Hill, North Carolina

Note: Sean C. Blackwell, MD, also contributed to this unit.

COLLEGE STAFF

Sterling B. Williams, MS, MD, PhD
Vice President for Education

Erica Bukevicz, MS, MBA
Senior Manager, Educational Development and Testing
Division of Education

Christopher T. George, MA
Editor, PROLOG

CONFLICT OF INTEREST DISCLOSURE

This PROLOG unit was developed under the direction of the PROLOG Advisory Committee and the Task Force for *Obstetrics*, Seventh Edition. PROLOG is planned and produced in accordance with the Standards for Enduring Materials of the Accreditation Council for Continuing Medical Education. Any discussion of unapproved use of products is clearly cited in the appropriate critique.

Current guidelines state that continuing medical education (CME) providers must ensure that CME activities are free from the control of any commercial interest. The task force and advisory committee members declare that neither they nor any business associate nor any member of their immediate families has material interest, financial interest, or other relationships with any company manufacturing commercial products relative to the topics included in this publication or with any provider of commercial services discussed in the unit except for **Bernard Gonik, MD**, who serves on advisory boards for Novartis, GSK, and Sanofi-Pasteur Vaccines, and serves as a speaker for Merck, GSK, and Sanofi-Pasteur; **Keith H. Nelson, MD**, who is a physician trainer for Implanon by Merck Pharmaceuticals; and **Linda Van Le, MD**, who serves on the speakers bureaus for Merck and Eisai and on the Advisory Board of Biologics, Inc. All potential conflicts have been resolved through the American College of Obstetricians and Gynecologist's mechanism for resolving potential and real conflicts of interest.

Preface

PROLOG (Personal Review of Learning in Obstetrics and Gynecology) is a voluntary, strictly confidential, self-evaluation program. PROLOG was developed specifically as a personal study resource for the practicing obstetrician–gynecologist. It is presented as a self-assessment mechanism that, with its accompanying performance information, should assist the physician in designing a personal, self-directed life-long learning program. It may be used as a valuable study tool, reference guide, and a means of attaining up-to-date information in the specialty. The content is carefully selected and presented in multiple-choice questions that are clinically oriented. The questions are designed to stimulate and challenge physicians in areas of medical care that they confront in their practices or when they work as consultant obstetrician–gynecologists.

PROLOG also provides the American College of Obstetricians and Gynecologists (the College) with one mechanism to identify the educational needs of the Fellows. Individual scores are reported only to the participant; however, cumulative performance data and evaluation comments obtained for each PROLOG unit help determine the direction for future educational programs offered by the College.

Process

The PROLOG series offers the most current information available in five areas of the specialty: obstetrics, gynecology and surgery, reproductive endocrinology and infertility, gynecologic oncology and critical care, and patient management in the office. A new PROLOG unit is produced annually, addressing one of those subject areas. *Obstetrics*, Seventh Edition, is the first unit in the seventh 5-year PROLOG series.

Each unit of PROLOG represents the efforts of a special task force of subject experts under the supervision of an advisory committee. PROLOG sets forth current information as viewed by recognized authorities in the field of women's health. This educational resource does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognized methods and techniques of clinical practice for consideration by obstetrician–gynecologists to incorporate in their practices. Variations of practice that take into account the needs of the individual patient, resources, and the limitations that are special to the institution or type of practice may be appropriate.

Each unit of PROLOG is presented as a two-part set, with performance information and cognate credit available to those who choose to submit their answer sheets for confidential scoring. The first part of the PROLOG set is the Assessment Book, which contains educational objectives for the unit and multiple-choice questions, and an answer sheet with return mailing envelope. Participants can work through the book at their own pace, choosing to use PROLOG as a closed- or open-book assessment. Return of the answer sheet for scoring is encouraged but voluntary.

The second part of PROLOG is the Critique Book, which reviews the educational objectives and items set forth in the Assessment Book and contains a discussion, or critique, of each item. The critique provides the rationale for correct and incorrect options. Current, accessible references are listed for each item.

Continuing Medical Education Credit

ACCME Accreditation

The American College of Obstetricians and Gynecologists is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

AMA PRA Category 1 Credit(s)™

The American College of Obstetricians and Gynecologists designates this enduring material for a maximum of 25 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

College Cognate Credit(s)

The American College of Obstetricians and Gynecologists designates this enduring material for a maximum of 25 Category 1 College Cognate Credits. The College has a reciprocity agreement with the American Medical Association that allows *AMA PRA Category 1 Credits*™ to be equivalent to College Cognate Credits.

Fellows who submit their answer sheets for scoring will be credited with 25 hours. Participants who return their answer sheets for CME credit will receive a Performance Report that provides a comparison of their scores with the scores of a sample group of physicians who have taken the unit as an examination. An individual may request credit only once for each unit. *Please allow 4–6 weeks to process answer sheets.*

Credit for PROLOG *Obstetrics*, Seventh Edition, is initially available through December 2015. During that year, the unit will be re-evaluated. If the content remains current, credit is extended for an additional 3 years, with credit for the unit automatically withdrawn after December 2018.

Conclusion

PROLOG was developed specifically as a personal study resource for the practicing obstetrician–gynecologist. It is presented as a self-assessment mechanism that, with its accompanying performance information, should assist the physician in designing a personal, self-directed learning program. The many quality resources developed by the College, as detailed each year in the College's *Publications and Educational Materials Catalog* are available to help fulfill the educational interests and needs that have been identified. PROLOG is not intended as a substitute for the certification or recertification programs of the American Board of Obstetrics and Gynecology.

PROLOG CME SCHEDULE

Gynecology and Surgery, Sixth Edition (2009)	Credit through 2014
Reproductive Endocrinology and Infertility, Sixth Edition (2010)	Credit through 2015
Gynecologic Oncology and Critical Care, Sixth Edition (2011)	Re-evaluated in 2013–Credit through 2016
Patient Management in the Office, Sixth Edition (2012)	Re-evaluated in 2014–Credit through 2017
Obstetrics, Seventh Edition (2013)	Re-evaluated in 2015–Credit through 2018

PROLOG Objectives

PROLOG is a voluntary, strictly confidential, personal continuing education resource that is designed to be both stimulating and enjoyable. By participating in PROLOG, obstetrician–gynecologists will be able to do the following:

- Review and update clinical knowledge.
- Recognize areas of knowledge and practice in which they excel, be stimulated to explore other areas of the specialty, and identify areas requiring further study.
- Plan continuing education activities in light of identified strengths and deficiencies.
- Compare and relate present knowledge and skills with those of other participants.
- Obtain continuing medical education credit, if desired.
- Have complete personal control of the setting and of the pace of the experience.

The obstetrician–gynecologist who completes *Obstetrics*, Seventh Edition, will be able to:

- Demonstrate an understanding of maternal and fetal physiology and pathophysiology and the effect on normal and complicated pregnancies.
- Identify components of antepartum care that optimize maternal and perinatal outcomes in uncomplicated pregnancies, including education regarding normal pregnancy.
- Diagnose and plan efficacious and cost-effective management of medical and obstetric conditions encountered during the antepartum period.
- Identify the risks and prognosis of selected complications of pregnancy and in the neonate.
- Describe invasive and noninvasive methods of fetal assessment in the antepartum period and identify the risks, indications, predictive value, and the physiologic basis for the tests.
- Diagnose problems and manage obstetric emergencies.
- Select appropriate management strategies for intrapartum care and delivery.
- Consider medical–legal principles, risk management and office management guidelines in obstetric practice.

Obstetrics, Seventh Edition, includes the following topics (item numbers appear in parentheses):

SCREENING AND DIAGNOSIS

Acute fatty liver of pregnancy (168–171)
Amniotic fluid embolus (109)
Anemia workup (33)
Aneuploidy screening (135–138)
Appendicitis in pregnancy (86)
Cerebral palsy (130)
Cervical insufficiency (96)
Chorioamnionitis (1)
Complications of anesthesia (70)
Complications of gastric bypass surgery in the obese parturient (59)
Diagnosis of fetal cytomegalovirus (32)
Diagnosis of parvovirus (53)
Disseminated intravascular coagulopathy (95)
Electronic fetal heart rate monitoring (100)
Fetal acid–base assessment (152–154)
Fetal hyperthyroidism (48)
Genetic screening in women of Ashkenazi Jewish descent (58)
Gestational diabetes mellitus (35)
Headache (73)
Hemoglobinopathy (155–159)

Hepatitis B (131–134)
Hepatitis C screening in pregnancy (94)
Hydramnios evaluation (101)
Imitators of severe preeclampsia (72)
Intimate partner violence (115)
Intrahepatic cholestasis of pregnancy (37)
Intrapartum electronic fetal monitoring nomenclature (144–148)
Macrosomia (3)
Maternal and fetal adverse effects of antihypertensives (9)
Maternal complications of sickle cell anemia (111)
Maternal hypothyroidism (116)
Monochorionic twins (91)
Motor vehicle collision (50)
Oligohydramnios (56)
Placental abruption (6)
Placenta previa at 20 weeks of gestation (106)
Positive antibody screen (26)
Pyelonephritis (88)
Screening for depression in pregnancy (23)
Screening testing strategies for fetal lung maturity (17)
Serum markers and adverse pregnancy outcome (28)
Thrombocytopenia (8)
Tuberculosis (54)
Twin–twin transfusion syndrome (85)
Ultrasonographic markers of Down syndrome (30)
Ultrasonography to date pregnancy (103)
Vaginal birth after cesarean delivery (98)
Vanity or keepsake ultrasonography (68)

MEDICAL MANAGEMENT

Anemia (74)
Antiphospholipid syndrome (19)
Asthma medications (61)
Breast mass in pregnancy (79)
Cerebral palsy (122, 128)
Cervical length (110, 117)
Cholestasis and fetal risks (75)
Chorioamnionitis (129)
Community-acquired pneumonia (25)
Contraindications to tocolysis (164–167)
Decreased fetal movement (36)
Fetal death (123)
Genital herpes in patient with preterm premature rupture of membranes (42)
Group B streptococci and penicillin allergy (44)
Hemolysis, elevated liver enzymes, and low platelet count syndrome (78)
Human immunodeficiency virus (45)
Hypertension in pregnancy (84)
Immunization in pregnancy (139–143)
Induction of labor (82, 118)
Inherited thrombophilia (113)
Intrahepatic cholestasis of pregnancy (20)
Intrauterine growth restriction (62)
Labor dystocia (10)
Latent phase of labor (105)

Management of thrombophilia (40)
Mastitis (66)
Migraine (127)
Mitral valve prolapse and subacute bacterial endocarditis (90)
Nausea and vomiting in pregnancy (108)
Patient in labor with human immunodeficiency virus (112)
Periodontal disease in pregnancy (49)
Peripartum anticoagulation (99)
Peripartum cardiomyopathy (39)
Postpartum fever (80)
Preterm premature rupture of membranes (24)
Prevention of recurrent preterm delivery (119)
Pulmonary embolism (67)
Recurrent spontaneous abortion (97)
Seizure disorder medications (102)
Severe rhesus disease in pregnancy (76)
Shoulder dystocia (65, 92)
Statins and drug exposure during pregnancy (34)
Steroid use in pregnancy (5)
Suppressive therapy for genital herpes (27)
Syphilis (2)
Thrombocytopenia (38)
Toxoplasmosis and pregnancy (43)
Treatment of gestational diabetes mellitus (41)
Tubal sterilization (77)
Use of biophysical profile in pregnancy management (120)
Use of vibroacoustic stimulation in pregnancy (22)
Uterine inversion (29)
Vulvar hematoma (12)

PHYSIOLOGY
Air travel (63)
Cardiovascular physiology (124)
Diabetes mellitus (121)

SURGICAL MANAGEMENT
External cephalic version (128)
Operative complications in the obese patient (11)
Postpartum hemorrhage (38)
Timing of antibiotic administration for cesarean delivery (104)

EPIDEMIOLOGY AND BIOSTATISTICS
Alcohol use in pregnancy (93)
Autoimmune disorders and pregnancy (52)
Cocaine use in pregnancy (18)
Congenital cytomegalovirus in pregnancy (126)
Congenital malformations due to methotrexate exposure (16)
Epidural complications (64)
Gestational diabetes mellitus recurrence (51)
Maternal and fetal adverse effects of tocolysis (149–151)
Maternal human immunodeficiency virus (83)
Perinatal survival (21)
Preterm birth (47)

COUNSELING
Contraindication to trial of labor after cesarean delivery (114)
Cystic fibrosis (125)
Fetal death (69)
Fish intake in pregnancy (107)
Influenza vaccination (57)
Management of triplets (46)
Multiple sclerosis (89)
Operative vaginal delivery (7)
Peripartum cardiomyopathy (81)
Prevention of listeriosis in pregnancy (13)
Smoking cessation (87)

ETHICAL AND LEGAL ISSUES
Elective cesarean delivery (14)
Hospital standards for neonatal resuscitation (55)
Legal and ethical obligations in patient transfer (71)
Periviable birth (60)
Postpartum contraception in new Centers for Disease Control and Prevention recommendations (15)
Steroid use in pregnancy (5)
Supplemental folic acid in the periconception period (4)
Use of peak flow meter in asthma (160–163)

A complete subject matter index appears at the end of the Critique Book.

1

Chorioamnionitis

An 18-year-old woman, gravida 1, para 0, at 41 weeks of gestation has had rupture of membranes for approximately 17 hours. She is in early labor with contractions every 5 minutes with cervical dilation at 5–6 cm. She received an epidural for pain relief 12 hours ago. Her temperature is 38.5° C (101°F). Her pulse is 124 beats per minute (bpm) and the fetal heart rate is 175 bpm with accelerations. She does not have any shortness of breath, dyspnea, or headaches. Her physical examination is notable for fundal tenderness. On admission, her white blood cell count was 18,000 cells/mm^3 and her urinalysis had negative leukocyte esterase and nitrites. The most likely cause of her fever is

(A) pyelonephritis
* (B) chorioamnionitis
(C) pneumonia
(D) epidural fever
(E) meningitis

Chorioamnionitis usually is diagnosed based on clinical findings of maternal fever, ie, temperature greater than 38.0°C (100.4°F), and at least two of the following: maternal tachycardia (pulse greater than 120 bpm), fetal tachycardia (greater than 160 bpm), uterine tenderness, or foul-smelling vaginal discharge. An increased white blood cell count greater than 15,000 cells/mm^3 is supportive of chorioamnionitis but not diagnostic.

Chorioamnionitis occurs in 0.5–10% of all pregnancies. Risk factors in term pregnancies include prolonged rupture of membranes, multiple digital examinations, placement of fetal scalp electrode or intrauterine pressure catheter, and prolonged labor.

Chorioamnionitis is most often polymicrobial and involves organisms from the vaginal flora, such as *Ureaplasma urealyticum*, *Mycoplasma hominis*, *Gardnerella vaginalis*, Gram-negative bacteria, and *Bacteroides species*. Colonization with group B streptococci and bacterial vaginosis also increase the risk.

Treatment of chorioamnionitis includes broad-spectrum antibiotics and supportive therapy. Cesarean delivery is not indicated for chorioamnionitis alone, unless there is presence of maternal or fetal compromise.

Differential diagnosis for acute chorioamnionitis includes pyelonephritis, pneumonia, epidural fever, and meningitis. Acute pyelonephritis complicates approximately 1–2.5% of pregnancies and has a recurrence rate of 10–18%. Along with fever and chills, symptoms often include dysuria, flank pain, urgency, and frequency. Approximately 10–20% of women are bacteremic.

Pyelonephritis can cause maternal and fetal tachycardia, especially if systemic involvement occurs. The most common pathogens are *Escherichia coli, Klebsiella pneumonia, Proteus* species, and group B streptococci. In the described case, the absence of positive leukocyte esterase and the absence of nitrites on urinalysis make pyelonephritis very unlikely. Pneumonia involves inflammation of lung tissue with consolidation and exudation. In the absence of any respiratory symptoms, it is unlikely as a source of intrapartum fever.

Epidural anesthesia has been associated with an increase in maternal fever in both observational studies and randomized controlled trials. Most often, the increase is minimal and confined to a low-grade temperature with no other signs of infection.

Meningitis and perispinal abscesses are extremely rare complications of epidural anesthesia. Along with fever, other common symptoms include headaches, nuchal rigidity, scotomata, nausea, and back pain. However, most cases do not develop until 24–48 hours after delivery.

Creasy R, Resnik R, Iams J, Lockwood C, Moore T, Greene M. Creasy and Resnik's maternal–fetal medicine: principles and practice. 6th ed. Philadelphia (PA): Saunders Elsevier; 2009. p. 757–9.

Newton ER. Chorioamnionitis and intraamniotic infection. Clin Obstet Gynecol 1993;36:795–808.

Segal S. Labor epidural analgesia and maternal fever. Anesth Analg 2010;111:1467–75.

Tita AT, Andrews WW. Diagnosis and management of clinical chorioamnionitis. Clin Perinatol 2010;37:339–54.

* Indicates correct answer.
Note: See Appendix A for a table of normal values for laboratory tests.

2
Syphilis

A 25-year-old woman, gravida 1, at 10 weeks of gestation comes to your office for prenatal care. Her rapid plasma reagin (RPR), non-specific treponemal antibody test was reactive with a titer of 1:16. She also had a positive treponemal specific test result. Other prenatal laboratory results were unremarkable. The patient has mild nausea but no other medical problems. She has a normal physical examination. She has a history of anaphylaxis with penicillin administration for streptococcal pharyngitis ("strep throat") 5 years ago, but she can tolerate cephalexin. The best treatment option is

(A) tetracycline
(B) azithromycin
* (C) penicillin G desensitization
(D) ceftriaxone

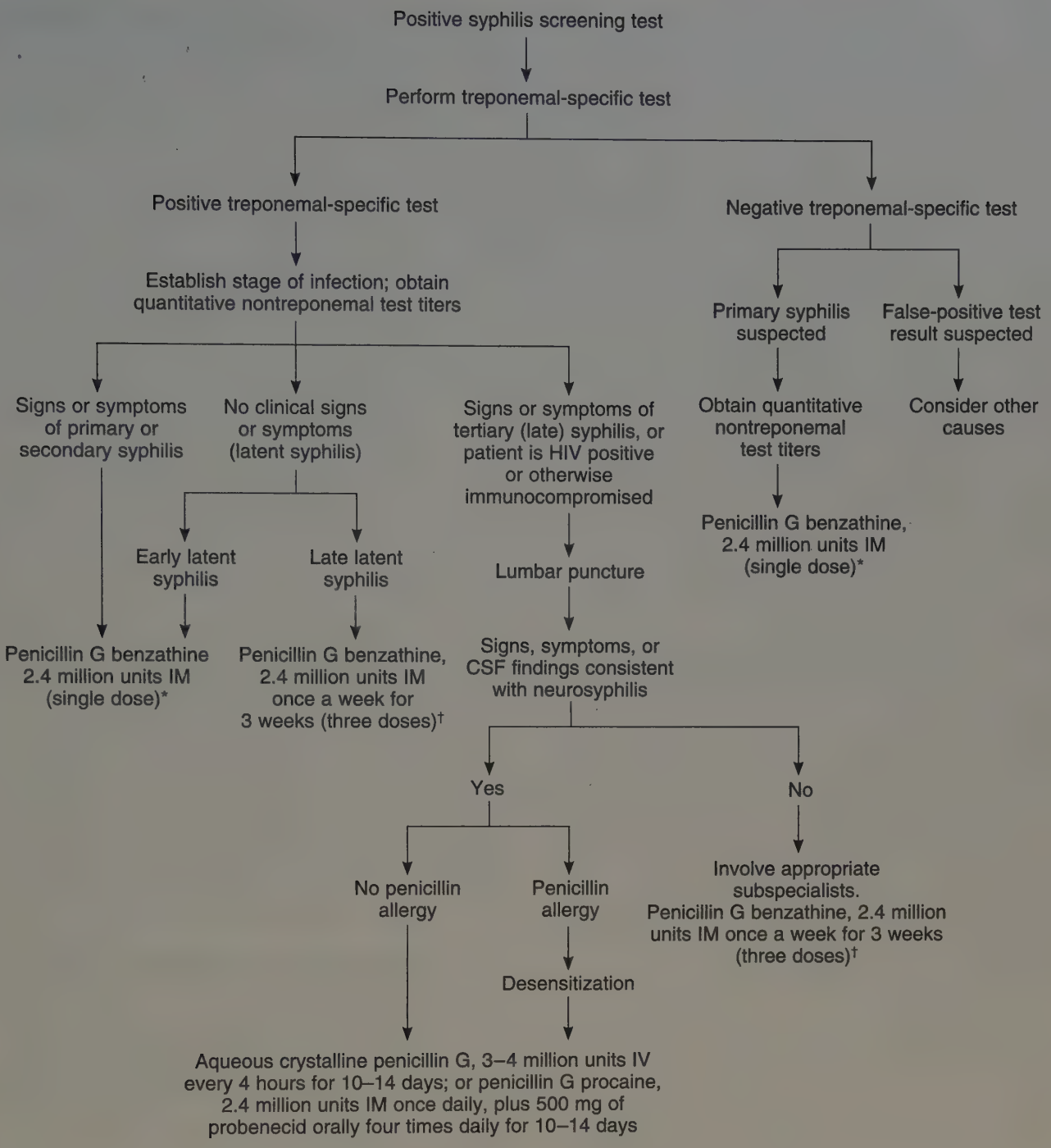
Treponema pallidum, a sexually transmitted spirochete, is the causative agent for syphilis. The initial infection is manifested by a painless primary ulcer or chancre, usually on the genitals (Fig. 2-1; see color plate), that appears 10–90 days (average 21 days) after infection and resolves over 4–6 weeks; 2–10 weeks later, secondary syphilis develops. The patient becomes symptomatic with headache, lymphadenopathy, fever, myalgia, fatigue, and rash. This resolves over 3–6 weeks, and if left untreated the disease enters a latency period with slow spirochete replication. Approximately 3–15 years after the initial infection, tertiary syphilis develops characterized by cardiac, late neurosyphilis, and gummatous destruction. Distinction is made regarding duration of treatment for patients with early syphilis of less than 1 year's duration and those with early syphilis beyond 1 year. Figure 2-2 shows an algorithm for recommended approaches to the treatment of syphilis.

It is known that *T pallidum* can cross the placenta and cause congenital syphilis in the fetus and newborn. The risk of vertical transmission from the mother to the newborn is approximately 60% with primary syphilis, nearly 100% with secondary syphilis, and 10% with latent syphilis. Manifestations of intrauterine infection include premature labor, hydrops fetalis, and fetal death. For the neonate, findings of congenital syphilis include snuffles (rhinorrhea), hepatosplenomegaly, rash, and low birth weight.

The U.S. Preventive Services Task Force recommends that all pregnant women be screened for syphilis to decrease the proportion of infants with clinical manifestations of syphilis infection. This usually is done during the first prenatal visit. The Centers for Disease Control and Prevention recommends repeat testing in the third trimester and at delivery for high-risk groups or individuals located in high incidence geographic locations. No infant should be discharged from the hospital without documentation of maternal syphilis status. Likewise all women with an intrauterine fetal demise should be screened for syphilis.

Although identification of spirochetes from syphilitic lesions or infected tissue indicates infection, screening usually is undertaken with a nontreponemal screening test, such as the Venereal Disease Research Laboratory (VDRL) test or the RPR test. False-positive results can occur with the VDRL and RPR tests from autoimmune disease, malignancy, other infections such as Lyme disease or Epstein–Barr virus, and pregnancy itself. During primary and secondary syphilis, the assay may provide a false-negative result if the assay is overwhelmed by large quantities of antibodies. This is termed the "prozone phenomenon" and can be corrected by dilution of the original sample. If the RPR or VDRL test is positive, the screening test is followed by a treponemal-specific test, such as a fluorescent treponemal antibody or *T pallidum* particle agglutination test. The enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction tests are being used in some settings, such as blood banking, for diagnosis of syphilis. Although ELISA tests have had limited studies in pregnancy, they have demonstrated 95% sensitivity and 99% specificity. This may be useful in the event of a false-positive RPR test result.

Parenteral administration of penicillin G is the best treatment for all stages of syphilis and is the only therapy with documented efficacy in pregnancy. Other antibiotic therapies for syphilis in penicillin allergic patients outside of pregnancy include tetracyclines, cephalosporins, and azithromycin. Because of adverse effects, resistance, and


Positive syphilis screening test
Perform treponemal-specific test
Positive treponemal-specific test
Negative treponemal-specific test
Establish stage of infection; obtain quantitative nontreponemal test titers
Primary syphilis suspected
False-positive test result suspected
Signs or symptoms of primary or secondary syphilis
No clinical signs or symptoms (latent syphilis)
Signs or symptoms of tertiary (late) syphilis, or patient is HIV positive or otherwise immunocompromised
Obtain quantitative nontreponemal test titers
Consider other causes
Penicillin G benzathine, 2.4 million units IM (single dose)*
Early latent syphilis
Late latent syphilis
Lumbar puncture
Penicillin G benzathine 2.4 million units IM (single dose)*
Penicillin G benzathine, 2.4 million units IM once a week for 3 weeks (three doses)†
Signs, symptoms, or CSF findings consistent with neurosyphilis
Yes
No
No penicillin allergy
Penicillin allergy
Involve appropriate subspecialists. Penicillin G benzathine, 2.4 million units IM once a week for 3 weeks (three doses)†
Desensitization
Aqueous crystalline penicillin G, 3–4 million units IV every 4 hours for 10–14 days; or penicillin G procaine, 2.4 million units IM once daily, plus 500 mg of probenecid orally four times daily for 10–14 days

*Alternative treatments for nonpregnant penicillin-allergic patients: doxycycline, 100 mg taken orally twice daily for 2 weeks, or tetracycline, 500 mg taken orally four times daily for 2 weeks; limited data support efficacy for ceftriaxone, 1 g once daily IM or IV for 8–10 days, or azithromycin, 2 g orally (single dose).

†Alternative treatments for nonpregnant penicillin-allergic patients: doxycycline, 100 mg taken orally twice daily for 4 weeks, or tetracycline, 500 mg taken orally four times daily for 4 weeks.

FIG. 2-2. Recommended approaches to the treatment of syphilis. Abbreviations: CSF, cerebrospinal fluid; HIV, human immunodeficiency virus; IM, intramuscular; IV, intravenous. (Brown DL, Frank JE. Diagnosis and management of syphilis. Am Fam Physician 2003;68:283–90. Based on information in Sexually transmitted diseases treatment guidelines 2002. Centers for Disease Control and Prevention. MMWR Morb Mortal Wkly Rep 2002:51(RR-6):18–25, 28–30.)

inadequate placental passage, these treatments are not considered adequate in pregnancy. The duration of penicillin therapy is usually one injection of 2.4 million units of benzathine penicillin G for early syphilis and three injections for syphilis of unknown duration (Table 2-1). The Jarisch–Herxheimer reaction is a febrile response to treatment of syphilis with penicillin that occurs 6–12 hours after treatment. It is not an allergic reaction and can be treated with antipyretics. It should not stop therapy.

The Centers for Disease Control and Prevention recommends that pregnant patients with documented penicillin allergy and syphilis infection undergo desensitization and treatment with penicillin G. Skin testing in monitored settings can help determine which patients have immunoglobulin E-mediated allergic reactions to penicillin. Desensitization can be accomplished with dilute penicillin formulations either intravenously or orally. This usually is done in a hospital setting over 4–12 hours after which the first full dose can be given. The patient must continue therapy until the penicillin course is completed or desensitization will need to be repeated.

For women who are incompletely treated or are treated less than 30 days before delivery, there remains concern for congenital syphilis. Abnormalities on the neonatal physical examination and fourfold higher titers on the neonate's RPR test result than the mother's titer raise concern for congenital syphilis. Long bone X-rays, auditory testing, and cerebrospinal fluid evaluation can assist in the diagnosis because the treponemal antibody is passed across the placenta and will make interpretation of the VDRL and RPR test results difficult. Treatment can prevent long-term consequences of congenital syphilis.

Congenital syphilis—United States, 2003–2008. Centers for Disease Control and Prevention. MMWR Morb Mortal Wkly Rep 2010;59:413–7.

Doroshenko A, Sherrard J, Pollard AJ. Syphilis in pregnancy and the neonatal period. Int J STD AIDS 2006;17:221,7; quiz 228.

Knight CS, Crum MA, Hardy RW. Evaluation of the LIAISON chemiluminescence immunoassay for diagnosis of syphilis. Clin Vaccine Immunol 2007;14:710–3.

Screening for syphilis infection in pregnancy: U.S. Preventive Services Task Force reaffirmation recommendation statement. U.S. Preventive Services Task Force. Ann Intern Med 2009;150:705–9.

Sutton MY, Dorell C. Syphilis. In: Global library for women's medicine. London: Foundation for the Global Library for Women's Medicine; 2009. Available at: http://www.glowm.com/?p=glowm.cml/section_view&articleid=30. Retrieved June 10, 2012.

Wendel GD Jr, Stark BJ, Jamison RB, Molina RD, Sullivan TJ. Penicillin allergy and desensitization in serious infections during pregnancy. N Engl J Med 1985;312:1229–32.

Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. Centers for Disease Control and Prevention [published erratum appears in MMWR Morb Mortal Wkly Rep 2011;60:18]. MMWR Recomm Rep 2010;59:1–110.

TABLE 2-1. Recommended Treatment for Pregnant Women With Syphilis

Category	Treatment
Early syphilis*	Benzathine penicillin G, 2.4 million units IM as a single injection; some recommend a second dose 1 week later
Syphilis of greater than 1 year duration†	Benzathine penicillin G, 2.4 million units IM weekly for three doses
Neurosyphilis‡	Aqueous crystalline penicillin G, 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion for 10–14 days or Procaine penicillin, 2.4 million units IM once daily, plus probenecid 500 mg orally 4 times daily, both for 10–14 days

Abbreviations: IM, intramuscular; IV, intravenous.

*Primary, secondary, and latent syphilis of less than 1-year duration.

†Latent syphilis of unknown or more than 1-year duration; tertiary syphilis.

‡Some recommend benzathine penicillin, 2.4 million units intramuscularly after completion of the neurosyphilis treatment regimens.

Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. Centers for Disease Control and Prevention [published erratum appears in MMWR Morb Mortal Wkly Rep 2011;60:18]. MMWR Recomm Rep 2010;59:1–110.

3

Macrosomia

A 28-year-old woman, gravida 2, para 1, comes to the office for a routine prenatal visit at 38 weeks of gestation. She started her pregnancy at a normal weight for her height and has gained 8.2 kg (18 lb) to date. Her first child was delivered vaginally at 39 weeks of gestation and weighed 3,750 g. Her 1-hour glucose tolerance test is normal. Her blood pressure is 110/70 mm Hg with a normal urinalysis. On physical examination, the fundal height is 39 cm and Leopold maneuvers suggest an infant in cephalic presentation that weights approximately 3,860 g (8.5 lb). The fetal heart rate is 130 beats per minute. Her cervix is closed, long, and firm. Ultrasonography shows a singleton pregnancy in cephalic presentation with an estimated fetal weight of 4,110 g (9 lb). The best next step in management is

(A) cesarean delivery at 39 weeks
* (B) expectant management
(C) immediate cesarean delivery
(D) immediate induction of labor
(E) induction of labor at 39 weeks

Macrosomia is a term that describes infants with birth weights in excess of 4,500 g. This definition is in contrast to fetuses considered large for gestational age, where growth is found to be in excess of the 90th percentile at any given gestational age. Considerable effort has been made to identify babies at risk of macrosomia in an attempt to decrease morbidity, especially morbidity associated with shoulder dystocia. Deliveries complicated by shoulder dystocia carry an increased risk of clavicular fracture, brachial plexus injury, depressed 5-minute Apgar scores, and increased admission rates to intensive care nurseries.

Estimation of fetal size is challenging. Clinical methods, including Leopold maneuvers and fundal height measurements, and maternal self-assessment, are as accurate as composite biometry measurements by ultrasonography when fetal weights exceed 4,000 g. Ultrasonographic systems typically calculate fetal weight based on several popular algorithms, such as the Hadlock formula, but most of these formulas are increasingly inaccurate in macrosomic fetuses. In one study, only one half of fetuses with birth weights greater than 4,500 g weighed within 10% of the estimated weight by ultrasonography.

Management of pregnancies with suspected macrosomia is also challenging. Maternal obesity and pregnancy weight gain strongly predict birth weight, but there are no randomized trials that assess diet for macrosomia prevention. In a meta-analysis of four randomized trials, dietary management of impaired glucose tolerance did not significantly decrease the number of infants with birth weights greater than 4,000 g. Labor induction in nondiabetic patients does not change the incidence of shoulder dystocia when macrosomia is suspected, but it does increase the rate of cesarean deliveries.

Cesarean delivery decreases but does not eliminate the risk of birth-related injuries, such as brachial plexus injury. Using ultrasonographic estimates of fetal weight greater than 4,250 g to recommend cesarean delivery did not significantly decrease shoulder dystocia nor eliminate birth-related trauma in the only observational study to evaluate this strategy. Multiple retrospective studies have shown low rates of vaginal birth-related injury, especially permanent birth-related injury, in infants with in utero weight estimates greater than 4,000–4,500 g. A cost analysis to examine cesarean delivery for macrosomic fetuses showed that the prevention of one permanent injury would require 3,695 operations at a cost of $8.7 million. The addition of diabetes mellitus to the analysis lowered the number of operations to 443 to prevent one permanent injury.

Economic analysis supports expectant management in pregnancies where macrosomia is suspected. In expectantly managed patients who enter labor spontaneously, attention should be paid to labor progress, with cesarean delivery in most cases preferred to instrumental delivery in the event of arrest of descent or prolonged second stage. Even in patients with previous cesarean delivery, macrosomia is not a contraindication to a trial of labor. At a fetal weight threshold of 5,000 g, or 4,500 g in mothers with diabetes mellitus, most authorities agree that primary cesarean delivery is a reasonable consideration, although the option is not supported with strong evidence. For these reasons, expectant management is the most appropriate initial management option for this case.

American College of Obstetricians and Gynecologists. Fetal macrosomia. ACOG Practice Bulletin 22. Washington, DC: ACOG; 2000.

Gherman RB, Chauhan S, Ouzounian JG, Lerner H, Gonik B, Goodwin TM. Shoulder dystocia: the unpreventable obstetric emergency with empiric management guidelines. Am J Obstet Gynecol 2006;195: 657–72.

Herbst MA. Treatment of suspected fetal macrosomia: a cost-effectiveness analysis. Am J Obstet Gynecol 2005;193:1035–9.

Sacks DA. Etiology, detection, and management of fetal macrosomia in pregnancies complicated by diabetes mellitus. Clin Obstet Gynecol 2007;50:980–9.

4

Supplemental folic acid in the periconception period

A 32-year-old woman is preparing for infertility treatment. You counsel her that she can reduce her risk of having a fetus with a neural tube defect (NTD) by taking a supplement that contains the micronutrient

(A) thiamine
* (B) folic acid
(C) pyridoxine
(D) beta carotene

Birth defects are the leading cause of infant mortality in the United States and are associated with 20.9% of neonatal deaths. The role of diet has been recognized as an environmental factor that influences the development of the embryo and fetus. Micronutrient deficiencies have been associated with reproductive risks from infertility, birth defects, and long-term diseases. The supplementation with micronutrients during pregnancy has been studied for a variety of pregnancy outcomes. Conclusive evidence is only available for periconceptional supplementation with folic acid to reduce the risks of NTDs. The prevention of other birth defects by supplementation of folic acid remains unclear. The role of supplemental folic acid in the prevention of congenital heart defects and other anomalies is under investigation. Studies are encouraging but inconclusive at this time because of limited numbers of participants and mixed results.

Neural tube defects are among the most common types of malformations. Such defects occur as a result of failure of the neural tube to close during the embryonic period. Malformations range from anencephaly to sacral meningomyelocele, depending on the location of the defect.

The embryo is most susceptible for the development of major malformation at 4–10 weeks of gestation (Fig. 4-1). The neural plate appears during the third week of gestation and gives rise to neural folds. The folds fuse in midline to form the neural tube. The closure of the neural tube occurs in multiple regions. Closure is complete by the sixth week of gestation. A patient's mean entry into prenatal care is at approximately 3 months of gestation when exposure to potential teratogens or opportunities to prevent defects through folic acid supplementation have already occurred. As a consequence, women of childbearing age should have these issues raised by a health care provider during the preconception period. A significant barrier to a preconception visit is that only approximately one half of the pregnancies in the United States are planned.

To address these issues, the U.S. Preventive Services Task Force in 1992 recommended that all women planning or capable of pregnancy should take a multivitamin supplement containing folic acid for the prevention of NTDs. The current recommended dosage is 0.4–0.8 mg. There is good evidence from randomized trials without fortification that a 0.8 mg supplement reduces the risk of NTDs. Observational studies report a reduction in NTDs in women taking a 0.4 mg supplement.

In 1996, the U.S. Food and Drug Administration mandated that all breads and grains sold in the United States be fortified with folic acid by January 1998. Recent data from national nutrition surveys and a March of Dimes Gallup poll survey report poor adherence to recommended folic acid intake. Less than 50% of women of childbearing age consume the appropriate levels of folic acid. Table 4-1 shows the folic acid content of selected foods. A recent study actually reported a decrease in folic acid intake. It was hypothesized that the reduction in intake was due to the popularity of low carbohydrate diets that are deficient in fortified foods. Even with food fortification in the United States, women are not ingesting enough to reach the recommended 0.4–0.8 mg intake

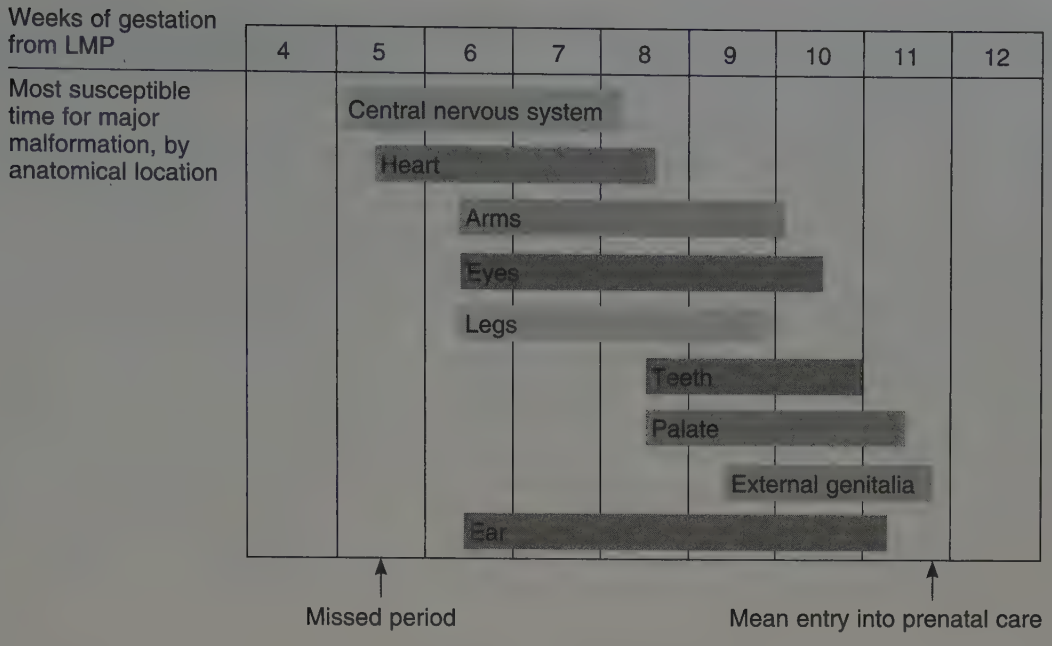


FIG. 4-1. Most susceptible times for major malformations by anatomical location and critical periods of development by weeks of gestation from last menstrual period (LMP).

TABLE 4-1. Selected Food Sources of Folate and Folic Acid

Food	Amount in mcg	Food	Amount in mcg
*Breakfast cereals fortified with 100% of the DV, ¾ cup	400	Broccoli, raw, 2 spears (each 5 in. long)	45
Beef liver, cooked, braised, 3 oz	185	Avocado, raw, all varieties, sliced, ½ cup sliced	45
Cowpeas (blackeyes), immature, cooked, boiled, ½ cup	105	Peanuts, all types, dry roasted, 1 oz	40
*Breakfast cereals, fortified with 25% of the DV, ¾ cup	100	Lettuce, romaine, shredded, ½ cup	40
Spinach, frozen, cooked, boiled, ½ cup	100	Wheat germ, crude, 2 tablespoons	40
Great northern beans, boiled, ½ cup	100	Tomato juice, canned, 6 oz	35
Asparagus, boiled, 4 spears	85	Orange juice, chilled, includes concentrate, ¾ cup	35
*Rice, white, long-grain, parboiled, enriched, cooked, ½ cup	65	Turnip greens, frozen, cooked, boiled, ½ cup	30
Vegetarian baked beans, canned, 1 cup	60	Orange, all commercial varieties, fresh, 1 small	30
Spinach, raw, 1 cup	60	*Bread, white, 1 slice	25
Green peas, frozen, boiled, ½ cup	50	*Bread, whole wheat, 1 slice	25
Broccoli, chopped, frozen, cooked, ½ cup	50	Egg, whole, raw, fresh, 1 large	25
*Egg noodles, cooked, enriched, ½ cup	50	Cantaloupe, raw, ¼ medium	25
		Papaya, raw, ½ cup cubes	25
		Banana, raw, 1 medium	20

* Items fortified with folic acid as part of the Folate Fortification Program.

Abbreviation: DV, daily value.

1 oz = 31.1 g; 1 in. = 2.54 cm.

Modified from National Institutes of Health. Office of Dietary Supplements. Dietary supplement fact sheet: folate. Bethesda (MD): NIH; 2009. Available at: http://ods.od.nih.gov/pdf/factsheets/Folate–HealthProfessional.pdf. Retrieved May 31, 2012.

without an additional supplement. Over-the-counter multivitamin supplements contain 0.4–0.8 mg or more of folic acid. Higher doses are empirically recommended for certain conditions, such as in women who have had a pregnancy with prior NTD (4 mg) and women who take some anticonvulsants.

Despite poor response rates to the recommendation for supplementation and fortification of foods, studies of serum folate levels have demonstrated that fewer people in the United States have low folate levels. In addition, a profound decrease has been observed in the number of pregnancies with high maternal serum alpha-fetoprotein levels along with a significant reduction in the prevalence of NTDs. Thiamine, pyridoxine, and beta-carotene have not been associated with a decrease in birth defects.

Cetin I, Berti C, Calabrese S. Role of micronutrients in the periconceptional period. Hum Reprod Update 2010;16:80–95.

Evans MI, Llurba E, Landsberger EJ, O'Brien JE, Harrison HH. Impact of folic acid fortification in the United States: markedly diminished high maternal serum alpha–fetoprotein values. Obstet Gynecol 2004;103:474–9.

Hobbs CA, Cleves MA, Karim MA, Zhao W, MacLeod SL. Maternal folate-related gene environment interactions and congenital heart defects. Obstet Gynecol 2010;116:316–22.

Jenkins KJ, Correa A, Feinstein JA, Botto L, Britt AE, Daniels SR, et al. Noninherited risk factors and congenital cardiovascular defects: current knowledge: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics. American Heart Association Council on Cardiovascular Disease in the Young. Circulation 2007;115:2995–3014.

Neural tube defects. ACOG Practice Bulletin No. 44. American College of Obstetricians and Gynecologists. Obstet Gynecol 2003;102:203–13.

Wolff T, Witkop CT, Miller T, Syed SB. Folic acid supplementation for the prevention of neural tube defects: an update of the evidence for the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality; 2009. Available at: http://www.uspreventiveservicestaskforce.org/uspstf09/folicacid/folicacides.pdf. Retrieved May 31, 2012.

5

Steroid use in pregnancy

A 24-year-old woman, gravida 4, para 0, at 29 weeks of gestation presents in preterm labor. Her cervix is 3 cm dilated and 80% effaced. Intact membranes are noted on speculum examination. The fetal heart rate tracing is Category I. You observe no evidence of chorioamnionitis. She was admitted 3 weeks ago for preterm labor and received a course of antenatal steroids. When she asks about further use of antenatal steroids, you tell her that the optimal number of additional courses of steroids is

* (A) 1
(B) 2
(C) 3
(D) 4

Administration of a single course of antenatal corticosteroids to women at risk of preterm birth is associated with a significant reduction in neonatal mortality, along with reductions in respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis without increasing the risk of maternal or neonatal morbidity or mortality. Antenatal corticosteroid exposure also is associated with a decreased rate of neonatal infectious morbidity, respiratory support, intensive care admission, and developmental delay. These benefits apply to women at 24 0/7–33 6/7 weeks of gestation, and are not limited by fetal sex or race.

Antenatal corticosteroids improve lung function and increase compliance by promotion of surfactant production; they also narrow the interalveolar septae, decrease vascular permeability, and enhance clearance of lung fluid. In the fetal brain, glucocorticoid exposure results in more mature neuronal communication and synaptic stabilization, but exposure may adversely affect brain development through inhibition of growth factors and impaired neural cell proliferation and myelination.

The American College of Obstetricians and Gynecologists (the College) recommends a single course of antenatal corticosteroids for pregnant women between 24 weeks and 34 weeks of gestation who are at risk of preterm delivery within 7 days. A single course of antenatal corticosteroids also is recommended for women with premature rupture of membranes before 32 weeks of gestation to reduce the risks of respiratory distress syndrome, perinatal mortality, and other morbidities. Use

before fetal age of viability is not recommended because of insufficient evidence on the efficacy of corticosteroids before this time.

A recent randomized clinical trial suggests that a single rescue course of antenatal corticosteroids may be considered if certain criteria are met. The criteria include women with a singleton or twin pregnancy with intact membranes at 25 0/7–32 6/7 weeks, judged to have a threat of preterm delivery within the next 7 days, and who received their first course of betamethasone before 30 weeks of gestation and at least 14 days before the intended rescue course. Compared with women given placebo, women who received a rescue course of betamethasone experienced a significant reduction in respiratory distress syndrome, need for surfactant, and composite neonatal morbidity. No evidence of an increased risk of neonatal complications or fetal growth restriction was identified in the rescue steroid-exposed group. Based on these data, a single rescue course of steroids is the best option for the described patient.

Regularly scheduled repeat courses of antenatal corticosteroids or multiple courses (more than two) are not recommended by the College because of potential maternal and fetal risk. Theoretical maternal risks include increased risk of infection and suppression of the hypothalamic–pituitary–adrenal axis. Fetal risks may include decreased birth weight and head circumference, fetal adrenal suppression, and an increased number of small for gestational age infants, especially after exposure to four courses of steroids. Although repeated courses of antenatal corticosteroids may be associated with a reduction in the rate and severity of respiratory distress syndrome, animal and human data suggest deleterious effects on the fetus regarding cerebral myelination, lung growth, and function of the hypothalamic–pituitary–adrenal axis.

Betamethasone and dexamethasone are the preferred corticosteroids for antenatal treatment to accelerate fetal organ maturation. Both cross the placenta and have similar biologic activity. A decreased incidence of intraventricular hemorrhage was identified with dexamethasone treatment in one report whereas a lower rate of adverse neurologic outcomes in infants at 18–22 months of age was noted after betamethasone exposure in another study. The College does not consider these limited data to be sufficient to recommend one steroid regimen over the other.

Antenatal corticosteroid therapy for fetal maturation. Committee Opinion No. 475. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:422–4.

Crowther CA, McKinlay CJD, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. Cochrane Database of Systematic Reviews 2011, Issue 6. Art. No.: CD003935. DOI: 10.1002/14651858.CD003935.pub3.

Eventov-Friedman S, Shinwell ES. Current controversies in perinatal steroid therapy. Acta Paediatr 2008;97:1492–501.

Garite TJ, Kurtzman J, Maurel K, Clark R. Impact of a 'rescue course' of antenatal corticosteroids: a multicenter randomized placebo-controlled trial. Obstetrix Collaborative Research Network. Am J Obstet Gynecol 2009;200:248.e1–9.

Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database of Systematic Reviews 2006, Issue 3. Art. No.: CD004454. DOI: 10.1002/14651858.CD004454.pub2.

Wapner RJ, Sorokin Y, Mele L, Johnson F, Dudley DJ, Spong CY, et al. Long-term outcomes after repeat doses of antenatal corticosteroids. National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. N Engl J Med 2007;357:1190–8.

6

Placental abruption

A 22-year-old primigravid woman at 31 weeks of gestation was admitted 5 days ago for preterm premature rupture of membranes. She is receiving antibiotics for latency and has completed a course of steroids. Her past medical history is negative. She smokes a half pack of cigarettes daily, but has been switched to a nicotine patch during the hospital stay. She now reports vaginal bleeding. When questioned, she reports that the baby is "balling up." Her heart rate is 110 beats per minute, blood pressure 130/80 mm Hg, and temperature 37.2°C (99.0°F). Fetal heart rate is 160 beats per minute with minimal variability. On abdominal examination, her uterus is continuously firm to palpation. Given this clinical scenario, the most likely diagnosis is

(A) placenta previa
(B) preterm labor
* (C) placental abruption
(D) chlamydial cervicitis

Placental abruption—the premature separation of a normally implanted placenta—complicates approximately 1% of births in the United States. It contributes to both preterm birth and perinatal death; the background risk of 8 perinatal deaths per 1,000 births is increased more than 10-fold to 119 perinatal deaths per 1,000 births when abruption is diagnosed. Multiple risk factors for abruption have been reported, including increasing maternal age and increasing parity, cigarette smoking, cocaine use, hypertensive disorders, premature rupture of membranes, chorioamnionitis, multiple gestations, and maternal trauma. Uterine factors (Müllerian anomalies, leiomyomas) are associated with an increased risk of abruption. An ultrasonographic diagnosis of subchorionic hematoma in early pregnancy is associated with a high risk of placental abruption later in the pregnancy. Previous abruption (in a prior pregnancy) increases the risk by 10–20-fold.

Signs and symptoms of abruption include vaginal bleeding, abdominal pain, increased uterine tone with frequent contractions, uterine tenderness, a uterus that is firm to palpation, and preterm labor. The absence of bleeding or pain does not exclude abruption as a diagnosis, because concealed bleeding may extravasate into the myometrium rather than out of the cervix. Fetal heart rate tracings may demonstrate bradycardia, sinusoidal pattern, reduced variability, or recurrent decelerations.

No laboratory test result is indicative of abruption. The Kleihauer-Betke test is neither sensitive nor specific for this diagnosis. Although coagulopathy is a complication, indices of coagulation do not change early enough to be useful for screening. More than 50% of coagulation factors are consumed before tests of coagulation depart from baseline. Ultrasonography is of limited use when abruption is suspected: sensitivity of ultrasonography for diagnosis is less than 25%. Thus, the diagnosis must still be established clinically in most cases. There is, however, a role for ultrasonography in excluding placenta previa as a cause of late-pregnancy bleeding. Because the diagnosis is not always obvious, a high index of suspicion for abruption should be maintained, especially in the setting of clinical risk factors. Additional pathology may coexist (eg, infection) but the presence of another condition does not preclude the possibility of abruption.

Maternal risks related to abruption are hemorrhage, hypovolemia, and complications that may be associated with hemorrhage, shock, coagulopathy, and renal failure. Fetal risks include preterm birth, stillbirth, and neurologic complications, such as intraventricular hemorrhage and periventricular leukomalacia.

Approximately 50% of abruptions occur before 37 weeks of gestation. Management of placental abruption depends on stability of the mother and the fetus, and gestational age attained. Mild cases remote from term may be observed for deterioration, whereas maternal or fetal compromise or a term gestational age should be taken as indications for delivery. Placental abruption does not preclude a trial of labor or an attempt at vaginal delivery, although the potential for maternal and fetal deterioration must be kept in mind, and careful monitoring is warranted. When undertaking labor, provisions for quick conversion to cesarean delivery, for transfusion, and for management of coagulopathy, must be made. Either coagulopathy or the development of a Couvelaire uterus (in which blood dissects into the myometrium and predisposes the patient to uterine atony) may necessitate massive transfusion or peripartum hysterectomy (Fig. 6-1; see color plate).

Ananth CV, Wilcox AJ. Placental abruption and perinatal mortality in the United States. Am J Epidemiol 2001;153:332–7.

Francois K, Foley MR. Antepartum and postpartum hemorrhage. In: Gabbe SG, Simpson JL, Niebyl JR, eds. Obstetrics: normal and problem

pregnancies. 5th ed. Philadelphia, PA: Churchill Livingston Elsevier; 2007. p. 456–85.

Glantz C, Purnell L. Clinical utility of sonography in the diagnosis and treatment of placental abruption. J Ultrasound Med 2002;21:837–40.

Hall DR. Abruptio placentae and disseminated intravascular coagulopathy. Semin Perinatol 2009;33:189–95.

Oyelese Y, Ananth CV. Placental abruption. Obstet Gynecol 2006; 108:1005–16.

Tikkanen M. Placental abruption: epidemiology, risk factors and consequences. Acta Obstet Gynecol Scand 2011;90:140–9.

Weiss HB, Sauber-Schatz EK, Cook LJ. The epidemiology of pregnancy-associated emergency department injury visits and their impact on birth outcomes. Accid Anal Prev 2008;40:1088–95.

7

Operative vaginal delivery

A 21-year-old primiparous woman at term has had an uncomplicated labor. She achieved complete dilation 3 hours ago. She has been pushing with contractions since then and the fetal head has descended to 3 cm below the maternal ischial spines with some caput. The presenting position is left occiput anterior. The fetal heart rate tracing is Category I. Estimated fetal weight is 3,800 g. Her epidural analgesia is functioning well. The patient reports that she is completely exhausted and requests an operative vaginal delivery. In counseling this patient for operative vaginal delivery by vacuum, you should inform her that the most serious complication related to use of this procedure is

* (A) subgaleal hemorrhage
(B) cephalohematoma
(C) facial palsy
(D) skull fracture

The incidence of operative vaginal delivery in the United States is approximately 10–15%; the procedure has been the subject of debate for the past 20 years. Some physicians feel the risks of operative vaginal delivery outweigh its benefits, but overall the evidence supports the practicality and safety of both forceps and vacuum delivery under the appropriate circumstances.

Prolonged second stage is no longer an absolute indication for operative vaginal delivery because there is no evidence that outcomes are improved by shortening the second stage, except for specific maternal or fetal indications, or unless no progress is being made. Box 7-1 lists the indications for operative vaginal delivery. In performing the procedure, the fetal head should be at least 2 cm below the ischial spine with no suspicion of cephalopelvic disproportion; the position of the head should be in an anteroposterior plane, right or left occiput anterior, or posterior position. For operative vaginal delivery by vacuum, the gestational age should be at least 34 weeks. The degree of station and lack of significant rotation from the anteroposterior plane is important because there is a strong correlation between these factors and increased risk, ie, the lower the fetal head and the less rotation required, the less the risk of both maternal and infant injury.

Retrospective studies and randomized trials have been quite reassuring that operative vaginal delivery does not carry a higher risk than cesarean delivery. The data are controversial in regard to risk of spontaneous vaginal delivery, with an elective low-forceps delivery carrying no immediate differences other than an increased incidence of maternal perineal trauma in primiparous women.

BOX 7-1

Indications for Operative Vaginal Delivery

No indication for operative vaginal delivery is absolute. The following indications apply when the fetal head is engaged and the cervix is fully dilated:

- Prolonged second stage:
  - — Nulliparous women: lack of continuing progress for 3 hours with regional anesthesia or 2 hours without regional anesthesia
  - — Multiparous women: lack of continuing progress for 2 hours with regional anesthesia or 1 hour without regional anesthesia
- Suspicion of immediate or potential fetal compromise.

American College of Obstetricians and Gynecologists. Operative vaginal delivery. ACOG Practice Bulletin 17. Washington, DC: ACOG; 2000.

Vacuum delivery carries different risks than forceps delivery. Cephalohematomas and subgaleal hematomas are more common with vacuum delivery (incidence 26–45 per 1,000 vacuum deliveries). Of the two types of hematoma, subgaleal hematoma is the more serious complication and often is associated with severe infant morbidity. Other vacuum delivery-associated risks include intracranial hemorrhage, hyperbilirubinemia, and retinal hemorrhage. Facial injury and skull fracture are not complications associated with vacuum delivery. Forceps delivery is more associated with corneal abrasions and external ocular trauma as well as facial bruising and maternal pelvic floor trauma. Although types of risks differ, the overall rate of injury does not appear to be significantly better with one delivery technique compared to the other. Therefore, health care providers are encouraged to use the type of delivery with which they are most comfortable or that is most appropriate to the immediate circumstances.

Although the data on the safety of operative vaginal delivery are reassuring, it is important to keep in mind the risks versus the benefits of the procedure. Overall, the incidence of serious complications with vacuum extraction is approximately 5%, and a similar incidence is observed for forceps delivery. This risk should be considered in conjunction with the benefit to be gained from shortening the patient's labor, or in contrast to the alternative of cesarean delivery if immediate delivery is indicated. This risk should be clearly communicated to the patient and the decision to intervene should be mutually made. For the described patient, subgaleal hemorrhage is the most severe complication associated with vacuum-assisted delivery. Cephalohematomas also may occur but are usually less severe.

Alexander JM, Leveno KJ, Hauth JC, Landon MB, Gilbert S, Spong CY, et al. Failed operative vaginal delivery. Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal–Fetal Medicine Units Network (MFMU). Obstet Gynecol 2009;114:1017–22.

American College of Obstetricians and Gynecologists. Operative vaginal delivery. ACOG Practice Bulletin 17. Washington, DC: ACOG; 2000.

Bofill JA, Rust OA, Schorr SJ, Brown RC, Martin RW, Martin JN Jr, et al. A randomized prospective trial of the obstetric forceps versus the M-cup vacuum extractor. Am J Obstet Gynecol 1996;175:1325–30.

Contag SA, Clifton RG, Bloom SL, Spong CY, Varner MW, Rouse DJ, et al. Neonatal outcomes and operative vaginal delivery versus cesarean delivery. Am J Perinatol 2010;27:493–9.

Fitzpatrick M, Behan M, O'Connell PR, O'Herlihy C. Randomised clinical trial to assess anal sphincter function following forceps or vacuum assisted vaginal delivery. BJOG 2003;110:424–9.

Towner D, Castro MA, Eby-Wilkens E, Gilbert WM. Effect of mode of delivery in nulliparous women on neonatal intracranial injury. N Engl J Med 1999;341:1709–14.

Yeomans ER. Operative vaginal delivery. Obstet Gynecol 2010; 115:645–53.

8

Thrombocytopenia

A patient comes to your office at 28 weeks of gestation for her 1-hour glucose tolerance test. A complete blood count is done at the same time. Her platelet count is 95,000/mm^3. A repeat platelet count 6 weeks later is 92,000/mm^3. She currently feels well with no recent illnesses. She is healthy and takes only a prenatal vitamin. Her initial prenatal laboratory results show a platelet count of 287,000/mm^3. She has normal blood pressure and her urine dipstick test result is negative for protein. The most likely diagnosis is

(A) preeclampsia
* (B) gestational thrombocytopenia
(C) idiopathic thrombocytopenia purpura
(D) drug-induced thrombocytopenia
(E) thrombocytopenia due to a viral illness

During pregnancy, maternal platelet counts are either unchanged or mildly decreased compared with a healthy nonpregnant patient. The mean platelet value in the third trimester is 213,000/mm^3. *Thrombocytopenia* is defined as a platelet count less than 150,000/mm^3. Thrombocytopenia is classified as

- mild, 100,000–150,000/mm^3
- moderate, 50,000–99,000/mm^3
- severe, less than 50,000/mm^3

The incidence of maternal thrombocytopenia at term is approximately 10%, but approximately 1% for moderate and severe thrombocytopenia.

Thrombocytopenia usually is diagnosed incidentally on a laboratory test and is less commonly detected because of a clinical presentation of bleeding or easy bruisability. Before a patient is given the diagnosis of thrombocytopenia and a workup is initiated, the health care provider must ensure that the low platelet count is not a laboratory error. A number of sampling errors may falsely lower the platelet count, such as platelet clumping in the blood sample. An automated count should be confirmed by a peripheral smear.

After thrombocytopenia has been confirmed, the health care provider should take a detailed history to narrow the differential diagnosis. Drug-induced thrombocytopenia, including herbal supplementation, such as quinine, is common and must be excluded. Thrombocytopenia usually occurs within the first month of drug initiation, and the patient generally recovers within 1 week after discontinuation of the drug.

A viral illness also can cause thrombocytopenia. In fact, thrombocytopenia may be the initial manifestation of human immunodeficiency virus (HIV) in 10% of patients, and eventually almost one half of patients with HIV will have thrombocytopenia. Medical disorders, such as systemic lupus erythematosus, disseminated intravascular coagulopathy, antiphospholipid syndrome, hypersplenism, myelodysplastic syndrome, hemolytic uremic syndrome, and thrombotic thrombocytopenic purpura, can cause thrombocytopenia. If all of the above causes of thrombocytopenia have been excluded in a nonpregnant patient, the most likely diagnosis is idiopathic thrombocytopenic purpura.

During pregnancy, thrombocytopenia can be caused by pregnancy-specific disorders. In fact, the etiology of thrombocytopenia in 75% of pregnant women is gestational thrombocytopenia, thus making it the most likely diagnosis in this patient. Gestational thrombocytopenia is suspected if the patient has no prior history of low platelets, the problem occurs during the mid-second trimester or later, and the platelet count is greater than 75,000/mm^3. Because gestational thrombocytopenia is so common, most physicians do not initiate a workup for other etiologies unless the patient's platelet count is less than 75,000/mm^3 or the patient's history is suggestive of another cause. The diagnosis is confirmed if the platelet count returns to normal in the postpartum period. Gestational thrombocytopenia is considered a self-limiting condition that should not affect obstetric management, except for possible concerns related to the administration of regional anesthesia. During pregnancy, gestational thrombocytopenia is difficult to distinguish from idiopathic thrombocytopenic purpura. Often the diagnosis of gestational thrombocytopenia is only confirmed after the platelet count returns to normal in the postpartum period.

Preeclampsia is another pregnancy-specific condition that can cause decreased platelets. Thrombocytopenia is usually not an isolated condition and is associated with other signs, such as hypertension, proteinuria, and elevated liver enzymes.

Boehlen F, Hohlfeld P, Extermann P, Perneger TV, de Moerloose P. Platelet count at term pregnancy: a reappraisal of the threshold. Obstet Gynecol 2000;95:29–33.

Gernsheimer T, McCrae KR. Immune thrombocytopenic purpura in pregnancy. Curr Opin Hematol 2007;14:574–80.

McCrae KR. Thrombocytopenia in pregnancy. Hematology 2010;2010: 397–402.

McCrae KR. Thrombocytopenia in pregnancy: differential diagnosis, pathogenesis, and management [published erratum appears in Blood Rev 2003;17:2]. Blood Rev 2003;17:7–14.

9

Maternal and fetal adverse effects of antihypertensives

A 30-year-old primigravid woman comes to your office for her first prenatal visit at 12 weeks of gestation. She has mild hypertension that has been treated with pharmacotherapy for the past year. She reports first-trimester exposure to an angiotensin converting enzyme (ACE) inhibitor. Her renal function is normal and she had a negative screen result for diabetes mellitus in the past year. The most appropriate next step to identify fetal abnormalities associated with ACE inhibitor therapy is

(A) karyotype
(B) nuchal translucency
(C) second-trimester serum screening
* (D) targeted ultrasonography

Shortly after the beginning of widespread use of ACE inhibitors for the treatment of chronic hypertension, it became apparent that use of these medications in the second trimester of pregnancy was associated with renal and skeletal anomalies and fetal death. First-trimester exposure was not thought to be a source of toxicity to the fetus. In the past 5 years, using administrative data, a teratogenicity signal for first-trimester exposure has been detected. It appears that exposure to ACE inhibitors in early pregnancy may be associated with an increased risk of congenital anomalies in the cardiovascular and central nervous systems. Karyotype, nuchal translucency, and second-trimester screening for aneuploidy do not detect abnormalities caused by ACE inhibitors. Thus, a targeted ultrasonographic study would be the diagnostic test of choice to assess for fetal abnormalities. The patient should stop using ACE inhibitors and be switched to another antihypertensive agent. No other class of drugs used to treat hypertension has such harmful fetal adverse effects as ACE inhibitors. Other options for treatment that are safe and effective include methyldopa, labetalol, and nifedipine. Angiotensin receptor blockers have uncertain safety in pregnancy and should be avoided.

Because hypertensive pregnant women have an increased risk of developing superimposed preeclampsia, and it is clinically difficult to discern between third-trimester increases in blood pressure and preeclampsia, many health care providers perform baseline laboratory testing in the first trimester. Laboratory tests often obtained include 24-hour urine collection for proteinuria quantification; measures of renal function, such as creatinine, blood urea nitrogen, and serum uric acid. These tests may be altered in mothers who develop preeclampsia-induced endothelial dysfunction.

The severity level of chronic hypertension at which pharmacologic therapy can improve perinatal outcomes remains unclear. Numerous clinical trials are ongoing to answer that question. Moreover, it is uncertain if treatment can delay or prevent the development of superimposed preeclampsia.

Briggs GG. Drug effects on the fetus and breast-fed infant. Clin Obstet Gynecol 2002;45:6–21.

Cooper WO, Hernandez-Diaz S, Arbogast PG, Dudley JA, Dyer S, Gideon PS, et al. Major congenital malformations after first–trimester exposure to ACE inhibitors. N Engl J Med 2006;354:2443–51.

Ilett KF, Kristensen JH. Drug use and breastfeeding. Expert Opin Drug Saf 2005;4:745–68.

Tabacova S, Little R, Tsong Y, Vega A, Kimmel CA. Adverse pregnancy outcomes associated with maternal enalapril antihypertensive treatment. Pharmacoepidemiol Drug Saf 2003;12:633–46.

10
Labor dystocia

A 19-year-old woman, gravida 1, is in spontaneous labor at 41 weeks of gestation. Initially, her cervix was 2 cm, 90% effaced, and the fetus was at –1 station. Clinical examination reveals an adequate maternal pelvis and an estimated fetal weight of 3,700 g. She receives oxytocin for labor augmentation. Her cervical examination progressed to 4 cm, 100% effacement, and 0 station, but has not changed for 2 hours and 20 minutes. The fetal heart rate tracing is Category I. An intrauterine pressure catheter is in place and she is contracting adequately on 20 mU/min of oxytocin. The best next step in management is

(A) cesarean delivery
(B) increase oxytocin
(C) add prostaglandin
* (D) continue labor

Historically, the definitions for normal and abnormal labor patterns used in clinical practice were derived from the seminal work of Dr. Emanuel A. Friedman. These limits of normal labor were based on the patterns of women who gave birth to normal infants in the 1950s at a single hospital and for whom there were no apparent labor complications and no epidural. However, in current practice, the natural course and management of labor is much different because of the heterogeneity of populations, the use of epidural anesthesia, lower rates of operative vaginal delivery, and the significantly higher rate of labor induction. The duration of the first stage is now considered to be much longer and the rate of cervical change in active labor is much slower.

The data from Dr. Friedman's study suggested that the shift from latent to active labor occurs between 3 cm and 4 cm. However, in a recent evaluation of the labor patterns of more than 26,000 women, it was noted that a large proportion of nulliparous women did not shift from latent to active labor until 6 cm, yet many multiparous women may undergo this shift even later (Fig. 10-1). It may take up to 4 hours for nulliparous women to change from 4 cm to 5 cm. In a study of a standardized labor induction protocol that required at least 12 hours of oxytocin after membrane rupture, a sizeable percentage of women who were in the latent phase of labor after 6–9 hours still experienced an uncomplicated vaginal birth.

Most likely, the described patient is still in latent labor and, therefore, labor arrest cannot be diagnosed at this time. Given the normal pelvimetry and estimated fetal weight, a diagnosis of fetopelvic disproportion is also unlikely. Thus, there is no indication for cesarean delivery at this time. Because the uterine contractions are adequate, increasing oxytocin dose is not warranted. Her labor pattern reflects that she is still in the latent phase, and continuation of labor without additional intervention is indicated.

Rouse DJ, Owen J, Hauth JC. Criteria for failed labor induction: prospective evaluation of a standardized protocol. Obstet Gynecol 2000;96:671–7.

Rouse DJ, Owen J, Savage KG, Hauth JC. Active phase labor arrest: revisiting the 2-hour minimum. Obstet Gynecol 2001;98:550–4.

Zhang J, Landy HJ, Branch DW, Burkman R, Haberman S, Gregory KD, et al. Contemporary patterns of spontaneous labor with normal neonatal outcomes. Consortium on Safe Labor. Obstet Gynecol 2010;116:1281–7.

Zhang J, Troendle J, Mikolajczyk R, Sundaram R, Beaver J, Fraser W. The natural history of the normal first stage of labor [published erratum appears in Obstet Gynecol 2010;116:196]. Obstet Gynecol 2010;115:705–10.

11

Operative complications in the obese patient

A 35-year-old woman, gravida 1, at 38 weeks of gestation requires a cesarean delivery for an active phase arrest. Her body mass index (calculated as weight in kilograms divided by height in meters squared [kg/m^2]) (BMI) is 45. She undergoes the cesarean delivery through a Pfannenstiel incision. The surgical technique or option that is most likely to prevent wound breakdown is

* (A) subcutaneous closure
(B) skin closure with staples
(C) placement of a subcutaneous drain
(D) to avoid electrocautery

Approximately 40% of reproductive-aged women in the United States are categorized as overweight or obese using BMI groupings. Obesity in pregnancy is a risk factor for multiple poor maternal, fetal, and neonatal outcomes. Elevated BMI is associated with high rates of gestational hypertension, preeclampsia, gestational diabetes mellitus, and fetal macrosomia. High rates of spontaneous abortion, fetal anomalies, and stillbirth also have been reported in women with high BMI. Cesarean delivery rates increase with increasing BMI. In women with BMI greater than 35, the cesarean delivery rate approaches 50%. The higher rates appear to be due to both labor abnormalities and fetal heart rate abnormalities.

Anesthetic complications are high in obese gravidas. Antepartum consultation with an anesthesiologist can be considered. If preexisting medical complications are present, such as hypertension, an electrocardiogram or other baseline evaluation may be helpful. Vascular access for intravenous placement in the obese patient can be challenging. Likewise, in obese women difficulties can be encountered with regional anesthesia with high rates of failed epidural placement. General anesthesia is more dangerous in the obese parturient with difficult intubation, high rates of aspiration, more rapid oxygen desaturation during intubation, and retention of lipid soluble anesthetic agents. Patient safety may be enhanced by keeping the patients without oral intake before surgery, use of antacids, and use of fiber-optic intubation equipment.

Planning for delivery of the obese patient should include consideration of appropriately engineered hospital beds and operating tables, and the availability of extra personnel for operative retraction and moving the patient if necessary. Obese patients have a longer cesarean delivery operative time, including a longer incision to delivery time and increased blood loss.

Location of the incision, subumbilical, supraumbilical, transverse, or vertical, has been the subject of debate, and the ideal type and location of incision has not been determined. A retrospective review suggests vertical incisions are associated with higher rates of wound breakdown. Others advocate transverse incisions as being less painful, promoting early ambulation, better inspiration, and coughing. Ultimately, tailoring the incision to the patient's body habitus and the surgeon's experience appears to be advisable. A Smead–Jones mass closure is preferred by some as a method to prevent dehiscence.

Wound infection and endometritis are common in obese patients who undergo cesarean delivery, and antibiotic prophylaxis should be used for cesarean delivery. A high dosage of prophylactic antibiotics has been suggested for obese women because of larger volume of distribution. The prophylactic antibiotic should preferably be administered before incision. Wound disruption occurs after 2.5–16% of cesarean deliveries and is a major source of perioperative morbidity. Careful hemostasis is desirable. Use of surgical electrocautery has raised concern over tissue devitalization and wound breakdown. Recent reviews in neurosurgery and general surgery have supported the safety of electrocautery. Subcutaneous wound drain placement studies have not consistently shown prevention of wound breakdown. In a meta-analysis of seven trials involving 2,056 women, there was decreased risk of hematoma, seroma (relative risk = 0.52) or composite wound complication (relative risk = 0.68) with subcutaneous closure in wounds. In a meta-analysis of five studies including 887 women where the depth of the incision was recorded, there appeared to be benefit of closure of subcutaneous tissue when the incision was at least 2 cm or deeper. The preferred surgical technique to prevent wound breakdown in the described patient would therefore be subcutaneous closure.

Delayed primary closure (leaving the skin and subcutaneous tissue open in the immediate postoperative period and closing the skin after an interval) is occasionally used for wounds that are traumatic, infected, or contaminated with bowel spillage. No systematic application of delayed

primary closure for a cesarean delivery in an obese patient is recommended. Closure of the skin with suture as compared with staples may be associated with a lower rate of cesarean wound breakdown in the general obstetric patient, although it has not been observed in the obese patient. Delayed removal of staples in the obese patient is suggested because of increased tension on the skin edge.

Obesity is a risk factor for postoperative venous thromboembolism. The optimal regimen for avoiding thrombosis in the perioperative period for the obese gravida has not been described. Early ambulation, regional anesthesia, sequential compression devices, and low dose heparin have all been used to prevent thrombotic disease.

Postpartum care for the obese woman should include counseling regarding diet and weight loss in the interpregnancy interval. Reports suggest generally improved pregnancy outcomes after weight loss related to bariatric surgery.

Anderson ER, Gates S. Techniques and materials for closure of the abdominal wall in caesarean section. Cochrane Database of Systematic Reviews 2004, Issue 4. Art. No.: CD004663. DOI: 10.1002/14651858.CD004663.pub2.

Antimicrobial prophylaxis for cesarean delivery: timing of administration. Committee Opinion No. 465. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:791–2.

Chelmow D, Rodriguez EJ, Sabatini MM. Suture closure of subcutaneous fat and wound disruption after cesarean delivery: a meta-analysis. 2004, Issue 5 Pt 1. Art. No.: PMID: 15121573; 103/5/974 [pii]. DOI: 10.1097/01.AOG.0000124807.76451.47.

Gates S, Anderson ER. Wound drainage for caesarean section. Cochrane Database of Systematic Reviews 2005, Issue 1. Art. No.: CD004549. DOI: 10.1002/14651858.CD004549.pub2.

Gunatilake RP, Perlow JH. Obesity and pregnancy: clinical management of the obese gravida. Am J Obstet Gynecol 2011;204:106–19.

Hall LF, Neubert AG. Obesity and pregnancy. Obstet Gynecol Surv 2005;60:253–60.

Obesity in pregnancy. ACOG Committee Opinion No. 315. American College of Obstetricians and Gynecologists. Obstet Gynecol 2005;106:671–5.

Olsen MA, Butler AM, Willers DM, Devkota P, Gross GA, Fraser VJ. Risk factors for surgical site infection after low transverse cesarean section. Infect Control Hosp Epidemiol 2008;29:477,84; discussion 485–6.

Weiss JL, Malone FD, Emig D, Ball RH, Nyberg DA, Comstock CH, et al. Obesity, obstetric complications and cesarean delivery rate—a population-based screening study. Am J Obstet Gynecol 2004;190: 1091–7.

12

Vulvar hematoma

A patient is seen 16 hours after she underwent a spontaneous vaginal delivery of a 4,138 g (9 lb 2 oz) infant and is noted to have a 6 × 5 cm right vulvar hematoma. She is uncomfortable and voiding is difficult. She is observed for 2 hours and the hematoma does not seem to be expanding. Her hematocrit is 30%, having decreased from a predelivery value of 36%, and her vital signs are stable. Rectovaginal examination reveals no hematoma. The best next step in management is

(A) incision and drainage of vulvar hematoma
(B) interventional radiology for embolization of pudendal vessels
(C) hypogastric artery ligation
* (D) observation
(E) blood transfusion

Vulvar hematomas occur in up to 5% of vaginal deliveries. They can be massive and conceal large blood loss within the upper genital tract and retroperitoneum. A stable vulvar hematoma that does not seem to be expanding in a woman with stable vital signs and hematocrit should be observed carefully. Many vulvar hematomas can be managed expectantly and do not require blood transfusion or intervention.

A rectovaginal examination will allow one to assess expansion in the perirectal, perivaginal, and retroperitoneal spaces. If the result of the examination is negative, observation would be a reasonable approach to management of this patient. In cases where the hematoma expands, management options include surgical re-exploration or pudendal artery embolization. Observation would include monitoring of vital signs, including serial observation of hematocrit levels. In this patient, blood transfusion is not needed given her hematocrit of 30%.

Interventional radiology offers the theoretical advantages of being minimally invasive and allowing selective embolization of the vessel that is supplying the hema-

toma. It also allows assessment of vessels below and above the urogenital diaphragm. It often is frustrating to open a vulvar hematoma, evacuate the clots, and be unable to identify the contributing vessel(s).

In scenarios where surgical exploration is chosen to treat an expanding hematoma and the bleeding blood vessel(s) cannot be identified, packing the vulva with sterile gauze is reasonable. The packing will compress damaged blood vessels and can be removed 12–24 hours later after coagulation has achieved hemostasis. Large retroperitoneal bleeds often require surgical exploration or interventional angiography to stop bleeding and cannot be treated with compression from below.

Benrubi G, Neuman C, Nuss RC, Thompson RJ. Vulvar and vaginal hematomas: a retrospective study of conservative versus operative management. South Med J 1987;80:991–4.

Propst AM, Thorp JM Jr. Traumatic vulvar hematomas: conservative versus surgical management. South Med J 1998;91:144–6.

Sheikh GN. Perinatal genital hematomas. Obstet Gynecol 1971;38: 571–5.

Villella J, Garry D, Levine G, Glanz S, Figueroa R, Maulik D. Postpartum angiographic embolization for vulvovaginal hematoma. A report of two cases. J Reprod Med 2001;46:65–7.

13

Prevention of listeriosis in pregnancy

A 39-year-old primigravid woman seeks nutritional advice at her first prenatal visit. Her sister had a fetal demise at 36 weeks of gestation that was attributed to infection with *Listeria monocytogenes*. She asks what foods she needs to avoid in order to decrease her risk of infection. You tell her that, in addition to avoiding unpasteurized food products, the type of food that she needs to avoid is

(A) canned tuna
(B) cream cheese
* (C) cold delicatessen meat
(D) canned salmon
(E) mozzarella cheese

Stillbirth is a major obstetric complication with a broad range of causes and risk factors. Although maternal infection with *L monocytogenes* is a rare cause of stillbirth, it is important because it is potentially preventable.

L monocytogenes is an intracellular facultative anaerobic, Gram-positive bacillus that causes illness in adults and children. Pregnant women are at increased risk. The increase in risk during pregnancy may be related to a relative immunosuppression during pregnancy and the placenta's susceptibility to the organisms. Infection with *L monocytogenes* usually is associated with eating contaminated food. Maternal symptoms are variable and can range from influenza-like symptoms or suspected food poisoning to sepsis, meningitis, or pneumonia. There is no reliable serologic evaluation and the diagnosis is made on culture of the organism.

In a pregnant woman, after ingestion, the bacterium crosses the intestinal cells into the bloodstream; it infects the placenta through hematogenous spread. In the placenta, multiple microabscesses develop that can be lethal to the fetus.

A woman can lower her risk of acquiring listeriosis by avoiding high-risk foods. The bacterium can grow at low temperatures so refrigeration does not always help. Cooking contaminated foods at high temperatures, however, does destroy the bacteria.

Delicatessen meat has been considered one of the highest risk food vehicles for listeriosis within the United States. Although some deli meat is pasteurized, contamination may be related to the food processing. An outbreak in 2002, related to contaminated turkey meat, resulted in 54 illnesses, including 8 deaths and 3 fetal deaths. In 2010, the U.S. Department of Agriculture, Food Safety and Inspection Service issued a recall of approximately 380,000 lb (172,365 kg) of deli meat that may have been contaminated at a food processing plant.

Other important sources of infection with *L monocytogenes* are food products made with unpasteurized milk. Cream cheese and mozzarella cheese may be consumed because they are made from pasteurized milk products. Canned salmon and tuna also may be safely eaten in moderation. The American College of Obstetricians and Gynecologists provides patients with nutritional guidance for pregnancy through its patient education materials. See Box 13-1 for standard recommendations for the prevention of listeriosis. Note that in addition to taking precautions

BOX 13-1

Prevention of Listeriosis

- Wash all fresh fruits and vegetables before consuming them.
- While pregnant, do not eat the following foods:
  - — Unpasteurized milk or soft cheeses
  - — Raw or undercooked meat, poultry, or shellfish
  - — Prepared meats, such as hot dogs or deli meats, unless they are heated until steaming hot
- Always be sure to wash your hands and any utensils, countertops, or cutting boards that have been in contact with uncooked meats.

with deli meat and dairy products, it is advisable to wash all fresh fruits and vegetables before consuming them. Recent reports have linked outbreaks of listeriosis with cantaloupe.

McClure EM, Goldenberg RL. Infection and stillbirth. Semin Fetal Neonatal Med 2009;14:182–9.

Posfay-Barbe KM, Wald ER. Listeriosis. Semin Fetal Neonatal Med 2009;14:228–33.

Reddy UM, Goldenberg R, Silver R, Smith GC, Pauli RM, Wapner RJ, et al. Stillbirth classification—developing an international consensus for research: executive summary of a National Institute of Child Health and Human Development workshop [published erratum appears in Obstet Gynecol 2010;115:191]. Obstet Gynecol 2009;114:901–14.

U.S. Department of Agriculture. Food Safety and Inspection Services. New York firm recalls deli meat products for possible Listeria contamination [press release]. Washington, DC: USDA; 2010. Available at: http://www.fsis.usda.gov/news_&_events/recall_049_2010_release/index.asp. Retrieved May 31, 2012.

14

Elective cesarean delivery

During a prenatal visit, a healthy 38-year-old primigravid woman asks about elective cesarean delivery. For personal reasons, she wants to plan her delivery to occur at 39 weeks of gestation. You review the relevant medical issues but are uncomfortable with agreeing to perform the cesarean delivery in the absence of a medical indication. The best option in this situation is to

(A) decline her request
* (B) refer her to another health care provider
(C) agree to perform the cesarean delivery
(D) offer elective induction

Elective cesarean delivery, also known as cesarean delivery on maternal request, cesarean on demand, patient-choice cesarean, or cesarean delivery in the absence of medical indications, first came to media attention at about the turn of the millennium. It is thought that rates of elective cesarean delivery might be as high as 2–5% of all births in the United States.

Cesarean delivery rates have been increasing over time and now account for one third of births in the United States. In other nations, those rates are even higher: in China, nearly 50% of births are by cesarean delivery. The population benefits of rates this high have never been confirmed. A U-shaped relationship exists between national or regional cesarean rates and adverse maternal outcomes.

In addition to the standard medical and obstetric factors that drive a decision for cesarean delivery, either the patient or health care provider may perceive a nonmedical indication for cesarean delivery. Such factors may include fear of pain, fear of childbirth, certainty of scheduling, or availability of the preferred obstetrician. In 2006, the National Institutes of Health convened a State of the Science conference to summarize trends, risks, benefits, and research directions relating to cesarean delivery on maternal request. In analyzing the available evidence, the panel compared planned prelabor cesarean delivery with planned vaginal birth, a construct that included labor that ended in unplanned cesarean deliveries. This is problematic because the decision to abandon labor and proceed instead to cesarean delivery is subject to a great deal of variation in practice, and the outcomes are affected by the prevailing cesarean delivery rate.

The quality of evidence was generally reported as weak or moderate. The panel stated that planned cesarean delivery suggested some benefit in terms of lower rates of postpartum hemorrhage, urinary incontinence, surgical or obstetric trauma, fetal mortality, neonatal central nervous system compromise, neonatal birth injury, and neonatal infection. However, this advantage was predicated on shorter gestations (ie, assumed elective cesarean delivery performed at 39 weeks, whereas pregnancies planned to

end as vaginal deliveries were allowed to continue for several weeks longer). In the analysis, the planned vaginal delivery group included women who had unplanned cesarean deliveries while in labor, a situation known to be consistent with higher rates of adverse outcomes than planned prelabor cesarean delivery. The panel concluded that the planned vaginal delivery group had lower rates of infection, anesthesia complications, placenta previa in subsequent pregnancy, subsequent infertility, neonatal respiratory morbidity, admission to neonatal intensive care units, and neonatal hospital stay. No consistent difference was shown between the two groups in anorectal function, sexual function, pelvic organ prolapse, postpartum pain, postpartum depression, thromboembolism, and maternal mortality. The panel cautioned that the quality of evidence, for the most part, was too poor to allow reliable judgements as to whether an outcome measure was better with planned cesarean or planned vaginal delivery. Nevertheless, the panel concluded, "Cesarean delivery upon maternal request may be a reasonable alternative to planned vaginal delivery. When a health care provider cannot support this request, it is appropriate to refer the woman to another health care provider."

The American College of Obstetricians and Gynecologists notes that women who desire several children are not good candidates for maternal request cesarean delivery. The International Federation of Gynecology and Obstetrics and the Society of Obstetricians and Gynaecologists of Canada, among others, state that cesarean delivery on maternal request cannot be justified and should not be offered.

Arguments have been put forward to create an ethical framework in which to consider cesarean delivery on maternal request. The argument from beneficence states that the physician's role is to favor clinical good over clinical harm when determining patient care; this balance may change as more data on the procedure become available. The justice-based argument holds that benefits and burdens must be fairly allocated. The concern is that the benefits of maternal request cesarean delivery may accrue for a few, whereas many others sustain either additional morbidity or a diversion of available health care resources. An argument based on autonomy is most commonly invoked to suggest that a patient has a right to request a treatment. However, this argument is invalid because it does not distinguish between negative rights—the absolute right to be left alone, ie, the right to refuse a recommended treatment—and positive rights, which require the actions of others to achieve the desired ends. The application of positive rights, in this setting, would suggest that physicians must always carry out patients' wishes, however medically invalid they may be. The extremes to which this idea might be carried are apparent. It follows that none of these arguments can be construed as creating a duty to offer maternal request.

However, patients may still request the procedure and health care providers are then obligated to respond. Many respected voices in obstetric ethics state that the health care provider's job is then to counsel the patient thoroughly about benefits and harms, and ask her to reconsider, but her continued wish may be honored. The health care provider who does not believe that this is an acceptable option should refer such a patient to a health care provider who will perform the procedure.

American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 394, December 2007. Cesarean delivery on maternal request. Obstet Gynecol 2007;110:1501.

International Federation of Gynecology and Obstetrics (FIGO). FIGO Committee for the Ethical Aspects of Human Reproduction and Women's Health. Ethical aspects regarding caesarean delivery for nonmedical reasons. In: FIGO, editor. Ethical issues in obstetrics and gynecology by the FIGO Committee for the Study of Ethical Aspects of Human Reproduction and Women's Health. revised ed. ed. London: FIGO; 2009. p. 72–3.

Joint policy statement on normal childbirth. Society of Obstetricians and Gynaecologists of Canada; Association of Women's Health, Obstetric and Neonatal Nurses of Canada; Canadian Association of Midwives; College of Family physicians of Canada; Society of Rural Physicians of Canada. JOGC J Obstet Gynaecol Can 2008;30:1163–5.

Minkoff H, Powderly KR, Chervenak F, McCullough LB. Ethical dimensions of elective primary cesarean delivery. Obstet Gynecol 2004;103:387–92.

National Institutes of Health state-of-the-science conference statement: Cesarean delivery on maternal request March 27–29, 2006. Obstet Gynecol 2006;107:1386–97.

Souza JP, Gulmezoglu A, Lumbiganon P, Laopaiboon M, Carroli G, Fawole B, et al. Caesarean section without medical indications is associated with an increased risk of adverse short-term maternal outcomes: the 2004–2008 WHO Global Survey on Maternal and Perinatal Health. WHO Global Survey on Maternal and Perinatal Health Research Group. BMC Med 2010;8:71.

Worley KC, McIntire DD, Leveno KJ. The prognosis for spontaneous labor in women with uncomplicated term pregnancies: implications for cesarean delivery on maternal request. Obstet Gynecol 2009;113:812–6.

15

Postpartum contraception in new Centers for Disease Control and Prevention recommendations

According to the 2011 Centers for Disease Control and Prevention recommendations, the use of combined oral contraceptives (OCs) can be safely started postpartum without contraindications at

(A) 2 days
(B) 7 days
(C) 14 days
* (D) 21 days
(E) 28 days

The risk of venous thromboembolism is increased during pregnancy and the postpartum period; the risk is most pronounced in the first weeks after delivery and decreases to near baseline levels by 42 days postpartum. Use of combined OCs increases the risk of venous thromboembolism in healthy reproductive-aged women; an additional risk might exist if used postpartum. There is no level 1 evidence that evaluates the risk of venous thromboembolism among postpartum women who use combined OCs. Risk of pregnancy during the first 21 days postpartum is low, but increases after that point; ovulation before first menses is common. Based on these considerations, the Centers for Disease Control and Prevention recommended in 2011 that women do not start combined OCs before 21 days postpartum.

This recommendation is similar for women who breastfeed or do not breastfeed their infants. The U.S. Department of Health and Human Services recommends that infants should be exclusively breastfed during the first 4–6 months of life, and preferably for a full 6 months. Ideally, breastfeeding should continue through the first year of life. Clinical studies demonstrate conflicting results about effects on milk volume in women exposed to combined OCs during lactation; no consistent effect on infant weight has been reported. Adverse health outcomes or manifestations of exogenous estrogen in infants exposed to combined OCs through breast milk have not been demonstrated. In general, these studies are of poor quality, lack standard definitions of breastfeeding or outcome measures, and have not included premature or ill infants. Theoretical concerns about the effects of combined OCs on breast milk production are greater in the early postpartum period when milk flow is being established and, therefore, it is recommended that women wait 21 days after giving birth before initiating the use of combined OCs.

Postpartum women may have other risk factors for venous thromboembolism, such as obesity, smoking, and temporary immobilization. In these women, use of combined OCs may be postponed at least until 42 days postpartum and full mobilization. In women with prior deep venous thrombosis, pulmonary embolism, or certain known thrombogenic mutations, use of combined OCs should be avoided, and alternatives discussed (Table 15-1).

TABLE 15-1. Summary of Recommendations and Risk Classifications* for Hormonal Contraceptive Methods and Intrauterine Devices During the Postpartum Period

Condition	COC/P/R	POP	DMPA	Implants	LNG–IUD	Cu–IUD
Postpartum (nonbreastfeeding women)						
a. Less than 21 days	4	1	1	1		
b. 21–42 days						
i. With other risk factors for VTE (such as age 35 years or more, previous VTE, thrombophilia, immobility, transfusion at delivery, BMI 30 or greater, postpartum hemorrhage, postcesarean delivery, preeclampsia or smoking)	3†	1	1	1		
ii. Without other risk factors for VTE	2	1	1	1		
c. Greater than 42 days	1	1	1	1		

(continued)

TABLE 15-1. Summary of Recommendations and Risk Classifications* for Hormonal Contraceptive Methods and Intrauterine Devices During the Postpartum Period *(continued)*

Condition	COC/P/R	POP	DMPA	Implants	LNG–IUD	Cu–IUD
Postpartum (breastfeeding women‡)						
a. Less than 21 days	4	2	2	2		
b. 21 days to less than 30 days						
i. With other risk factors for VTE (such as age 35 years or more, previous VTE, thrombophilia, immobility, transfusion at delivery, BMI 30 or greater, postpartum hemorrhage, postcesarean delivery, preeclampsia or smoking)	3†	2	2	2		
ii. Without other risk factors for VTE	3	2	2	2		
c. 30–42 days						
i. With other risk factors for VTE (such as age 35 years or more, previous VTE, thrombophilia, immobility, transfusion at delivery, BMI 30 or greater, postpartum hemorrhage, postcesarean delivery, preeclampsia or smoking)	3†	1	1	1		
ii. Without other risk factors for VTE	2	1	1	1		
d. Greater than 42 days	2	1	1	1		
Postpartum (breastfeeding or nonbreastfeeding women, including postcesarean delivery)						
a. Less than 10 minutes after delivery of the placenta					2	1
b. 10 min after delivery of the placenta to less than 4 weeks					2	2
c. 4 weeks or greater					1	1
d. Puerperal sepsis					4	4

Abbreviations: BMI, body mass index (weight in kilograms divided by height in meters squared [kg/m^2]); COC, combined oral contraceptive; Cu–IUD, copper-bearing IUD; DMPA, depot medroxyprogesterone acetate; IUD, intrauterine device; LNG–IUD, levonorgestrel-releasing IUD; P, combined hormonal patch; POP, progestin-only pill; R, combined vaginal ring; VTE, venous thromboembolism.

*Categories: 1, a condition for which there is no restriction for the use of the contraceptive method; 2, a condition for which the advantages of using the method generally outweigh the theoretical or proven risks; 3, a condition for which the theoretical or proven risks usually outweigh the advantages of using the method; 4, a condition that represents an unacceptable health risk if the contraceptive method is used.

†For women with other risk factors for VTE, these risk factors might increase the classification to "4" (eg, smoking, deep venous thrombosis–pulmonary embolism, known thrombogenic mutations, and peripartum cardiomyopathy).

‡The breastfeeding recommendations are divided by month in *U.S. Medical Eligibility Criteria for Contraceptive Use*, 2010. They have been divided by days for purposes of integration with the postpartum recommendations.

Update to CDC's U.S. Medical Eligibility Criteria for Contraceptive Use, 2010: revised recommendations for the use of contraceptive methods during the postpartum period. Centers for Disease Control and Prevention. MMWR Morb Mortal Wkly Rep 2011;60:878–83.

Espey E, Ogburn T, Leeman L, Singh R, Ostrom K, Schrader R. Effect of progestin compared with combined oral contraceptive pills on lactation: a randomized controlled trial. Obstet Gynecol 2012;119:5–13.

Update to CDC's U.S. Medical Eligibility Criteria for Contraceptive Use, 2010: revised recommendations for the use of contraceptive methods during the postpartum period. Centers for Disease Control and Prevention. MMWR Morb Mortal Wkly Rep 2011;60:878–83.

16

Congenital malformations due to methotrexate exposure

A patient was treated with methotrexate for a suspected ectopic pregnancy. She returns to the clinic 4 weeks later with nausea and vomiting, breast tenderness, and a positive pregnancy test result. Ultrasonography reveals an intrauterine 10-week-sized fetus. As her physician, you inform her that methotrexate exposure during pregnancy is associated with

(A) no major anomalies
(B) congenital renal anomalies
(C) anomalies that are preventable with folic acid supplementation
(D) anomalies that are preventable with leucovorin rescue
* (E) limb and cranial anomalies

Methotrexate is an antimetabolite chemotherapeutic agent. It binds to dihydrofolate reductase and blocks the reduction of dihydrofolate to tetrahydrofolic acid, the active form of folic acid. Therefore, methotrexate specifically works as a folic acid antagonist. Ultimately, methotrexate disturbs DNA, RNA, and protein synthesis. Undesired adverse effects of methotrexate include bone marrow suppression as well as liver, lung, and renal toxicity.

Systemic methotrexate has been used to treat gestational trophoblastic disease since 1956. Methotrexate is used today to treat a variety of other malignancies, such as acute lymphoid and myeloid leukemia, breast cancer, Hodgkin disease, and bone osteosarcoma. Methotrexate also is used to treat other conditions, such as rheumatoid arthritis, Crohn disease, severe psoriasis, systemic lupus erythematosus, and ectopic pregnancy. As the clinical indications for methotrexate treatment have broadened, the chance of fetal exposure has increased in reproductive-aged women.

Methotrexate is used to treat ectopic pregnancies and as an abortifacient. When used in these clinical scenarios, methotrexate exposure does not appear to interfere with subsequent fertility or cause abnormalities in future pregnancies. A limited number of studies have suggested that conception within 6 months of exposure does not cause different outcomes than in patients who conceived more than 6 months after being exposed to methotrexate. The recommended interval between treatment with methotrexate and conception to decrease any potential risk has not been well established.

Methotrexate exposure during pregnancy is associated with fetal abnormalities. The most characteristic abnormalities induced by methotrexate include abnormal head shape, large fontanelles, craniosynostosis, ocular hypertelorism, and limb defects. Developmental delay and intellectual impairment also may occur. The frequency of congenital anomalies associated with methotrexate exposure has not been determined, and this makes counseling problematic. The likelihood that an abnormality will occur is probably related to the dose of methotrexate as well as to the timing of administration during embryogenesis. Exposure later in the second or third trimester of pregnancy may be associated with intrauterine growth restriction and not anomalies. The described patient should be counseled regarding the potential risk of exposure during pregnancy.

Folic acid supplementation is recommended for all women of reproductive age but supplementation after fetal exposure to methotrexate has not been shown to prevent fetal anomalies. Leucovorin counteracts the toxic adverse effects of high-dose methotrexate but is not recommended for the prevention of birth defects after methotrexate exposure.

Chapa JB, Hibbard JU, Weber EM, Abramowicz JS, Verp MS. Prenatal diagnosis of methotrexate embryopathy. Obstet Gynecol 2003;101:1104–7.

Medical management of ectopic pregnancy. ACOG Practice Bulletin No. 94. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008;111:1479–85.

Micromedex® Healthcare Series [Internet database]. Methotrexate sodium. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Available at http://www.micromedex.com. Accessed November 16, 2011.

Nguyen C, Duhl AJ, Escallon CS, Blakemore KJ. Multiple anomalies in a fetus exposed to low-dose methotrexate in the first trimester. Obstet Gynecol 2002;99:599–602.

Svirsky R, Rozovski U, Vaknin Z, Pansky M, Schneider D, Halperin R. The safety of conception occurring shortly after methotrexate treatment of an ectopic pregnancy. Reprod Toxicol 2009;27:85–7.

Usta IM, Nassar AH, Yunis KA, Abu-Musa AA. Methotrexate embryopathy after therapy for misdiagnosed ectopic pregnancy. Int J Gynaecol Obstet 2007;99:253–5.

17

Screening testing strategies for fetal lung maturity

A 31-year-old woman, gravida 3, para 2, comes to your clinic for a routine prenatal visit at 39 weeks of gestation. She enrolled late for prenatal care at 28 weeks of gestation. To date, she has had an uncomplicated pregnancy with normal weight gain, fetal growth, and laboratory testing. On examination, the fetus is in cephalic presentation and her cervix is favorable. She requests labor induction before her husband is deployed next week for military service. Amniocentesis is performed. Analysis of the blood-contaminated amniotic fluid shows a lecithin–sphingomyelin ratio of 1.7 and the presence of phosphatidylglycerol. The best management option for this patient is

(A) amniocentesis in 1 week
(B) corticosteroid therapy
* (C) immediate labor induction
(D) labor induction in 1 week
(E) lamellar body count testing

Fetal lung maturity testing is indicated when scheduled delivery is considered in the absence of specific criteria that establish a gestational age greater than 39 weeks, unless the delivery is planned for maternal or fetal indications. Historic criteria that can establish presumed fetal lung maturity are the following:

- Ultrasonographic measurement at less than 20 weeks of gestation support a gestational age of 39 weeks or greater
- Fetal heart tones have been documented as present for 30 weeks by Doppler ultrasonography
- It has been 36 weeks since a positive serum or urine human chorionic gonadotropin pregnancy test result

The goal of these criteria is to avoid iatrogenic causes of respiratory distress syndrome (RDS) and other complications of prematurity in the infant. One of the most avoidable scenarios for iatrogenic RDS is scheduled cesarean delivery, whether by maternal request or by planned repeat procedure. In infants born by elective cesarean delivery between 37 0/7 weeks and 38 6/7 weeks of gestation, the rate of RDS was 25 in 1,000 live births, compared with a rate of 7 in 1,000 live births in infants born after 39 0/7 weeks of gestation. Even in cases where pulmonary maturity is established by testing, delivery before 39 0/7 weeks of gestation is associated with increased morbidity in the neonate. In this case, amniocentesis is indicated because the patient enrolled late for prenatal care and does not meet the historic criteria for fetal maturity.

Fetal lung maturity testing evaluates either the presence or function of phospholipids that form surfactant in the fetal lungs. Surfactant formation in the fetal lungs is one of several processes that, if interrupted or incomplete, relates to potential lung disease in the newborn. Surfactant, released from lamellar bodies in type II pneumocytes, reduces surface tension in the alveolus and optimizes gas exchange. Lecithin is the most common phospholipid and appears earlier than other types, including phosphatidylinositol and phosphatidylglycerol. When surfactant is deficient, alveolar surface tension is higher, which leads to alveolar collapse and inhibits gas exchange. The result is RDS, demonstrated by hypoxia, acidosis, and increased shunting in the lungs. Serious complications, both immediate and chronic, are associated with RDS, including necrotizing enterocolitis, patent ductus arteriosus, intraventricular hemorrhage, infection, and chronic lung disease. Other processes also may cause difficulty with ex utero respiratory exchange.

The tests available for fetal lung maturity evaluation are described in Table 17-1. In 2010, the manufacturer announced that they would no longer produce the reagents or analyzer for the TDx–FLM II, a fetal lung maturity assay that measures surfactant–albumin ratios by fluorescence polarization. The decision to replace the aging platform removes a widely available, rapid, and relatively simple lung maturity test from the arsenal available to the obstetrician. Testing for the lecithin–sphingomyelin ratio is another commonly used assay. Such testing is technically demanding and time-consuming, and the result must be interpreted in light of local standards depending on specimen processing. For example, centrifugation of the amniotic fluid can remove contaminants, such as blood and mucus, but also may remove surfactant, so the threshold for maturity may be lower.

Of the available tests, only testing for phosphatidylglycerol is not affected by the presence of blood. In the described patient, phosphatidylglycerol is present. Accordingly, with this mature fetal lung maturity test result, immediate delivery may be offered. Given the high negative predictive value for all of the available tests for

TABLE 17-1. Commonly Used Direct Tests of Fetal Lung Maturity

Test*	Technique	Time and Ease of Testing†	Threshold	Typical Predictive Value (%)		Contamination Effect		
				Mature Negative Predictive Value	Immature Positive‡ Predictive Value	Blood Affects Result?	Meconium Affects Result?	Vaginal Pool Sample?
Lecithin–sphingomyelin ratio	Thin-layer chromatography	++++	2–3.5	95–100	33–50	Yes	Yes	Yes
Phosphatidyl-glycerol	Thin-layer chromatography	++++	Present (usually 3% of total phospholipid)	95–100	23–53	No	No	Yes
Phosphatidyl-glycerol	Antisera with AmnioStat–FLM	+	0.5 = low positive 2 = high positive	95–100	23–53	No	No	Yes
Lamellar body counts	Commercial hematology counter	++	30,000–40,000 (investigational)	97–98	29–35	Yes	No	Not available
Optical density at 650 nm	Spectrophotometer	+	Optical density of 0.15 or greater	98	13	Not available	Not available	Not available
Foam stability index	Ethanol added to amniotic fluid, shaken, presence of bubbles at meniscus noted	++	47–48 or greater	95	51	Yes	Yes	No
Fluorescence polarization	Fluorescence polarization with TDx–FLM II	+	55 mg/g or greater of albumin§	96–100	47–61	Yes	Yes	Yes

*Commercial versions are available for all tests except optical density and lamellar body counts. Commercial availability of fluorescence polarization ended in 2010.

†Range in complexity: (+) indicates procedure is simple, available all the time, short, and not labor-intensive; (++++) indicates procedure is complex or difficult, time-consuming, and often not available all the time.

‡Positive predictive value is the probability of neonatal respiratory distress syndrome when the fetal lung maturity test result is immature.

§The manufacturer reformulated the product and testing procedure. The original assay threshold was 70; the more recent discontinued threshold

fetal lung maturity, discrepant results (in which one test is positive and another negative) should not dissuade an indicated delivery. Neither repeat amniocentesis nor corticosteroid therapy would offer any benefit, and lamellar body counts are potentially inaccurate in the presence of blood.

Alternative strategies for new and existing fetal lung maturity testing continue to be explored. Critics of the existing recommendations for fetal lung maturity testing suggest modifying the cutoff value for maturity with a gestational age-specific threshold. Many authors have examined the relationship between fetal lung maturity and ultrasonographic findings. A biparietal diameter greater than or equal to 9.2 cm has been correlated with a high probability of fetal lung maturity. More recently, an investigation of fetal pulmonary artery Doppler velocimetry showed an inverse correlation between the acceleration-time/ejection-time ratio and the amniotic fluid lecithin/sphingomyelin ratio.

Azpurua H, Norwitz ER, Campbell KH, Funai EF, Pettker CM, Kleine M, et al. Acceleration/ejection time ratio in the fetal pulmonary artery predicts fetal lung maturity. Am J Obstet Gynecol 2010;203:40.e1–8.

Bates E, Rouse DJ, Mann ML, Chapman V, Carlo WA, Tita AT. Neonatal outcomes after demonstrated fetal lung maturity before 39 weeks of gestation. Obstet Gynecol 2010;116:1288–95.

Luo G, Norwitz ER. Revisiting amniocentesis for fetal lung maturity after 36 weeks' gestation. Rev Obstet Gynecol 2008;1:61–8.

Tita AT, Landon MB, Spong CY, Lai Y, Leveno KJ, Varner MW, et al. Timing of elective repeat cesarean delivery at term and neonatal outcomes. Eunice Kennedy Shriver NICHD Maternal–Fetal Medicine Units Network. N Engl J Med 2009;360:111–20.

18

Cocaine use in pregnancy

A 27-year-old woman, para 0, at 27 weeks of gestation gives birth to a 1,100-g fetus after a rapid labor complicated by heavy uterine bleeding. Her urine toxicology test result is positive. The most likely drug use associated with this clinical scenario is

(A) opiate
* (B) cocaine
(C) marijuana
(D) barbiturate
(E) benzodiazepine

Illicit drug use is common in reproductive-aged women. At least 14% of women aged 15–44 years in the United States have used cocaine. Although illicit drug use in pregnancy is lower than use among nonpregnant women of reproductive age, approximately 4.5% of pregnant women report illicit use of drugs. Cocaine is the third most common drug used by pregnant women in the United States after marijuana and nonmedical use of prescription drugs.

Cocaine is a potent stimulant that exerts its actions by blocking the reuptake of the neurotransmitters dopamine, norepinephrine, and serotonin at the presynaptic level. These actions lead to increased catecholamine levels and enhanced sympathetic responses that cause vasoconstriction, hypertension, and tachycardia. Users of cocaine experience agitation and euphoria. Cocaine is believed to cross the placenta by simple diffusion because of its properties of high water content, lipid solubility, low molecular weight, and low ionization at physiologic pH.

Numerous adverse perinatal effects have been associated with cocaine use in pregnancy. Associations with cocaine use include increased risks of low birth weight, preterm birth, and intrauterine growth restriction. Pregnant cocaine users are also at increased risk of placental abruption. Abruption is thought to be mediated through the drug's hypertensive and vasoconstrictive effects. Prenatal cocaine exposure has been associated with effects on offspring. Changes in infant arousal, school age behavioral problems, and a need for special education have all been reported. Functional neuroimaging has demonstrated differences in areas of the brain involved in regulation of attention and response inhibition. Studies suggest that the cognitive ability termed "executive function" is affected by prenatal cocaine exposure.

Fetal effects may be mediated through decreased placental blood flow, which may reduce the supply of oxygen and nutrients to the fetus, or through direct effects of cocaine on the fetal vasculature. Cocaine also may act as an intrauterine stressor that alters fetal programming through epigenetic mechanisms, which causes changes in the developing fetal neuroendocrine and neurotransmitter systems.

Associations of adverse outcomes must be tempered by the difficulty in isolating cocaine's effects in humans. Numerous confounders exist, such as cigarette use, other drugs, socioeconomic status, lack of prenatal care, and poor nutrition. In addition, assessment of cocaine's effects on outcome is complicated by the various methods of consumption and the unknown amount of drug ingested.

The use of methamphetamine has been increasing since the 1980s, especially in the Western and Midwestern United States. Similar to cocaine, it is a potent stimulant producing an intense euphoria and has a longer half-life. Effects on pregnancy and infant outcomes are less well studied than those of cocaine. The risk of abruption is unclear but may be increased as with cocaine based on their similar mechanism of action. Although opiates, barbiturates, marijuana, and benzodiazepines have been associated with other perinatal complications, placental abruption has not been associated with them.

Gouin K, Murphy K, Shah PS. Effects of cocaine use during pregnancy on low birthweight and preterm birth: systematic review and metaanalyses. Knowledge Synthesis group on Determinants of Low Birth Weight and Preterm Births. Am J Obstet Gynecol 2011;204:340.e1–12.

Methamphetamine abuse in women of reproductive age. Committee Opinion No. 479. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:751–5.

National Survey on Drug Use and Health (U.S.). Results from the 2009 National Survey on Drug Use and Health. Rockville (MD): Dept. of Health and Human Services, Substance Abuse and Mental Health Services Administration, Office of Applied Studies; 2010. Available at: http://oas.samhsa.gov/NSDUH/2k9NSDUH/2k9ResultsP.pdf. Retrieved August 3, 2011.

Rayburn WF. Maternal and fetal effects from substance use. Clin Perinatol 2007;34:559,71, vi.

Salisbury AL, Ponder KL, Padbury JF, Lester BM. Fetal effects of psychoactive drugs. Clin Perinatol 2009;36:595–619.

19

Antiphospholipid syndrome

A 26-year-old woman, gravida 3, is at 14 weeks of gestation. Both of her previous pregnancies resulted in a pregnancy loss in the second trimester. She also developed a pulmonary embolus during the postpartum period. She had positive test results for anticardiolipin antibody and lupus anticoagulant. In addition to administration of low-dose aspirin, the most appropriate medical therapy for her during pregnancy and the postpartum period is

* (A) heparin
(B) folic acid
(C) steroids
(D) no additional therapy

Pregnant women with antiphospholipid syndrome are at increased risk of thromboembolism and certain adverse outcomes, such as pregnancy loss, preeclampsia, and fetal growth restriction. The risk of thrombosis in pregnancy or the postpartum period is approximately 5–12%; most of the cases are venous thromboembolisms (65–70%).

The purpose of medical treatment for antiphospholipid syndrome is to prevent thromboembolism and improve perinatal outcomes. Anticoagulation therapy is indicated when the laboratory and clinical criteria for antiphospholipid syndrome are present (See Appendix B). Treatment would be continued through the postpartum period (ie, past 6 weeks after delivery) because of the increased risks of thromboembolism during this time. In most treatment studies of antiphospholipid syndrome, in addition to being prescribed heparin, most women received low-dose aspirin.

Drug therapy often is started early in pregnancy, at pregnancy confirmation or at the end of the first trimester, and continued until after delivery. Given the concern about risk of increased bleeding and potential complications, some anesthesiologists may discontinue low-dose aspirin 7–10 days before delivery; however, there is a lack of scientific evidence to support such discontinuation of aspirin therapy. Anticoagulation therapy is administered either with unfractionated heparin or low molecular weight heparin. In many women with antiphospholipid syndrome, the timing of delivery is planned (ie, scheduled induction or cesarean delivery) and efforts are made to discontinue the anticoagulation therapy 1 day before delivery. Treatment with anticoagulation can be restarted 6 hours after vaginal delivery and 12 hours after cesarean delivery if significant bleeding has not occurred.

The described patient meets the clinical and laboratory criteria for antiphospholipid syndrome. She should be treated with heparin and baby aspirin. Neither folic acid nor steroids are used in the treatment of this syndrome.

Antiphospholipid syndrome. Practice Bulletin No. 118. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:192–9.

Bates SM, Greer IA, Pabinger I, Sofaer S, Hirsh J. Venous thromboembolism, thrombophilia, antithrombotic therapy, and pregnancy: American College of Chest Physicians Evidence–Based Clinical Practice Guidelines (8th Edition). American College of Chest Physicians. Chest 2008;133:844S–86S.

Horlocker TT, Wedel DJ, Benzon H, Brown DL, Enneking FK, Heit JA, et al. Regional anesthesia in the anticoagulated patient: defining the risks (the second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation). Reg Anesth Pain Med 2003;28:172–97.

Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295–306.

20

Intrahepatic cholestasis of pregnancy

A 36-year-old woman, gravida 4, para 2, at 34 weeks of gestation presents with a 1-week history of severe full body pruritus that is significantly affecting her sleep. The itching involves her palms and soles, but there is no associated rash. Laboratory findings show mildly increased liver function tests and an increased serum bile acid level. The best next step in management is to administer

(A) cholestyramine
(B) dexamethasone
(C) S-adenosyl-L-methionine
* (D) ursodeoxycholic acid

Intrahepatic cholestasis of pregnancy complicates up to 1% of pregnancies in the United States but is more common in Latin American and South Asian populations, in women with multiple gestations, pregnancies after in vitro fertilization, hepatitis C-positive women, and patients older than 35 years. The pathophysiology of the disease involves impaired clearance of bile acids and bilirubin in response to increased levels of estrogen and progesterone.

The classic presentation involves persistent total-body pruritus that commonly starts in the palms and soles and develops after the 30th week of gestation. Itching becomes progressively severe with advancing gestational age, has a nocturnal predominance, and often precedes laboratory abnormalities. Skin rash is characteristically absent in intrahepatic cholestasis of pregnancy. Pruritus usually improves soon after delivery but recurs in 40–60% of subsequent pregnancies. The administration of estrogen–progestin oral contraceptives to women with a history of intrahepatic cholestasis of pregnancy rarely results in recurrent cholestasis. Thus, oral contraception with a low-dose of estrogen can be initiated after normalization of liver function tests. However, women should be informed of the possible risks of pruritus or cholestasis. Elevated total serum bile acid concentration is commonly the first and sometimes the only laboratory abnormality seen in intrahepatic cholestasis of pregnancy. Mildly increased transaminase levels are common although levels of up to 1,000 international units/L may be seen. Hyperbilirubinemia is present in up to 25% of cases but levels rarely exceed 6 mg/dL.

Intrahepatic cholestasis of pregnancy poses little risk to maternal health. Conversely, the disease is associated with an increased risk of preterm delivery, abnormal fetal testing, meconium-stained fluid, and fetal demise. The risk of adverse fetal outcome appears to increase with higher bile acid levels, especially once a level of 40 micromol/L is achieved.

The treatment goal for intrahepatic cholestasis of pregnancy is to reduce maternal symptoms and minimize adverse fetal outcome. Ursodeoxycholic acid more effectively reduces pruritus and bile acid levels than cholestyramine, dexamethasone, and S-adenosyl-L-methionine. The effect of ursodeoxycholic acid on perinatal outcome is less clear, although a decreased rate of preterm delivery has been reported in several trials. Adverse maternal and fetal effects from ursodeoxycholic acid have not been reported. Antihistamines, such as hydroxyzine, may improve pruritus and insomnia but do not appear to affect bile acid levels or fetal outcome. Ursodeoxycholic acid is considered the drug of choice for this condition.

Despite reports of fetal demise that occurs within days of a reactive nonstress test, once-weekly or twice-weekly fetal testing is routinely recommended from the time of diagnosis until delivery. Daily fetal kick counting is another form of noninvasive surveillance that may be employed.

Immediate delivery is not indicated because of the risks associated with preterm birth, including respiratory distress syndrome. To minimize the risk of prematurity and fetal demise, which occurs at a median gestational age of 38 weeks, delivery at or near term is commonly recommended.

Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. World J Gastroenterol 2009;15:2049–66.

Glantz A, Marschall HU, Mattsson LA. Intrahepatic cholestasis of pregnancy: relationships between bile acid levels and fetal complication rates. Hepatology 2004;40:467–74.

Pathak B, Sheibani L, Lee RH. Cholestasis of pregnancy. Obstet Gynecol Clin North Am 2010;37:269–82.

Saleh MM, Abdo KR. Intrahepatic cholestasis of pregnancy: review of the literature and evaluation of current evidence. J Womens Health (Larchmt) 2007;16:833–41.

21

Perinatal survival

A patient presents at 24 weeks of gestation in active labor with a cervical dilation of 8 cm and breech presentation. You deem that delivery is imminent and that cesarean delivery would be the best option for the fetus. The fetal factor that is most predictive of the survival of the preterm newborn is

(A) race
(B) gender
(C) birth weight
* (D) gestational age

Gestational age is the fetal factor that is most predictive of survival of a preterm newborn. Race, gender, estimated fetal weight, and use of corticosteroids all influence the likelihood of survival in an extremely premature infant. The independent contribution that each of these factors makes to survival estimates can be calculated using the online calculator at the National Institute of Child Health and Human Development web site (Box 21-1). This risk calculator uses data from a research network of neonatal centers in the United States to provide risk estimates for extremely preterm newborns. One can enter gestational age and race, gender, birth weight, and use of corticosteroids to obtain a tailored risk estimate. The hope is that this information will be used by health care providers and patients for decision making. Despite the availability of such risk estimates, it is unclear whether improved prediction helps families or health care providers in their decision making.

Survival is not the only outcome parents of extremely preterm babies should factor into their decision making. Lifelong sequelae for the child's lungs, brain, and vision are common in surviving children. Moreover, minor deficits in motor and cognitive condition occur more frequently as these tiny newborns age. The online calculator (Box 21-1) provides parents and health care providers with prevalence estimates of major disabilities in infants who survive preterm birth.

Gibson AT. Outcome following preterm birth. Best Pract Res Clin Obstet Gynaecol 2007;21:869–82.

Reeves SA, Gibbs RS, Clark SL. Magnesium for fetal neuroprotection. Am J Obstet Gynecol 2011;204:202.e1–4.

Wang Y, Tanbo T, Ellingsen L, Abyholm T, Henriksen T. Effect of pregestational maternal, obstetric and perinatal factors on neonatal outcome in extreme prematurity. Arch Gynecol Obstet 2011;284:1381–7.

Watts JL, Saigal S. Outcome of extreme prematurity: as information increases so do the dilemmas. Arch Dis Child Fetal Neonatal Ed 2006;91:F221–5.

BOX 21-1

National Institute of Child Health and Human Development Neonatal Research Network's Online Calculator to Enable Calculation of Survival From Extremely Preterm Birth Outcome Data

Can I use the data to determine individual outcomes?

- These data are not intended to be predictive of individual infant outcomes. Instead, the data provide a range of possible outcomes based on specific characteristics.
- If you choose to use these data to determine possible outcomes, please remember that the information provided is not intended to be the sole basis for care decisions, nor is it intended to be a definitive prediction of outcomes if intensive care is provided. Users should keep in mind that every infant is an individual, and that factors beyond those used to formulate these standardized assessments may influence an infant's outcomes.
- Enter the characteristics below.

Gestational Age (Best Obstetric Estimate in Completed Weeks):

Select—

- 22 weeks
- 23 weeks
- 24 weeks
- 25 weeks

Birth Weight (401–1,000 grams): ___ grams

Sex: ❑ Female ❑ Male

Singleton Birth: ❑ Yes ❑ No

Antenatal Corticosteroids (Within 7 Days Before Delivery): ❑ Yes ❑ No

Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD). NICHD Neonatal Research Network (NRN): Extremely Preterm Birth Outcome Data. Available at http://www.nichd.nih.gov/about/org/cdbpm/pp/prog_epbo/epbo_case.cfm. Accessed June 8, 2012.

22

Use of vibroacoustic stimulation in pregnancy

Vibroacoustic stimulation is most useful as an adjunct to the antepartum nonstress test when the test is

(A) reactive with variable decelerations
(B) reactive with late decelerations
* (C) nonreactive without decelerations
(D) nonreactive with late decelerations

The nonstress test is the most frequently used assessment of antepartum fetal well-being during the third trimester. It is based on the premise that a fetus with normal acid–base status will have fetal heart rate accelerations coupled with fetal movements. A *reactive nonstress test result* is defined as two episodes of accelerations of 15 beats per minute above baseline that last for at least 15 seconds in a 20-minute period (after 32 weeks gestation). The presence of a reactive nonstress test result is associated with a very low risk of stillbirth (0.6%) in the next 7 days. Approximately 10–12% of all nonstress tests will remain nonreactive at 30 minutes and 6% will remain nonreactive at 40 minutes. The most common reason for a nonreactive stress test result near to term is that the fetus is in the quiet sleep state (1F or 3F). A third trimester fetus may spend up to 40% of its time in the quiet sleep state. Other causes of a nonreactive nonstress test result include central nervous system depression due to fetal acidemia and maternal narcotic use.

Vibroacoustic stimulation is performed with use of an artificial larynx with a vibrating disc. It is positioned on the maternal abdomen and a stimulus of 1–2 seconds is applied, which may be repeated up to three times as necessary. There is no advantage to using vibroacoustic stimulation more than three times. If the fetus is in the quiet sleep state, this stimulus will induce a behavioral change. If an acceleration occurs, it has the same predictive meaning as a spontaneous acceleration. The main advantage of the use of vibroacoustic stimulation in antepartum testing is that it can shorten the time to achieve a reactive nonstress test result by up to 10–20 minutes without compromising the detection of an acidotic fetus. Fetuses that develop a deceleration in response to vibroacoustic stimulation are at an increased risk of adverse perinatal outcomes and require further evaluation.

The most useful circumstance for vibroacoustic stimulation is in the presence of a nonreactive nonstress test result without any decelerations. A reactive nonstress test result does not need an adjunct test, such as vibroacoustic stimulation. The presence of decelerations during a nonstress test, whether variable or late, often require use of a back-up test, such as a biophysical profile in which amniotic fluid volume and other fetal parameters can be assessed.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. ACOG Practice Bulletin 9. Washington, DC: ACOG; 1999.

Clark SL, Sabey P, Jolley K. Nonstress testing with acoustic stimulation and amniotic fluid volume assessment: 5973 tests without unexpected fetal death. Am J Obstet Gynecol 1989;160:694–7.

Dunston–Boone G, Kuhlman K, Kaufmann M. Correlation of fetal heart rate decelerations following acoustic stimulation with perinatal outcome. Am J Perinatol 1995;12:342–6.

Smith CV, Phelan JP, Broussard P, Paul RH. Fetal acoustic stimulation testing. III. Predictive value of a reactive test. J Reprod Med 1988;33:217–8.

Smith CV, Phelan JP, Platt LD, Broussard P, Paul RH. Fetal acoustic stimulation testing. II. A randomized clinical comparison with the nonstress test. Am J Obstet Gynecol 1986;155:131–4.

23

Screening for depression in pregnancy

A 25-year-old woman, gravida 1, para 1, had an uncomplicated vaginal delivery. At her 6-week postpartum visit, she tells you that she is worried about postpartum depression, which she has read about in a newspaper. She is currently without depressive symptoms and on no medications. In regard to the patient's concern about postpartum depression, the best next step in management is

* (A) to screen with the Edinburgh Postnatal Depression Scale
(B) to start prophylactic paroxetine
(C) for the health care provider to initiate a mood assessment
(D) to refer to a psychiatrist
(E) to recommend self-monitoring

Clinical depression is extremely common in women. It is estimated that one in seven women receives treatment for the condition, and it is likely that many other women do not seek treatment. The World Health Organization identifies depression as a leading cause of disability in women. Postpartum depression carries some unique features, but appears to be a variant of the broader diagnosis of depression rather than a unique disease.

Several excellent depression screening tools are available. These tools are brief, easily completed by a variety of patients, well-validated in many clinical settings, and simple for the busy health care provider to interpret. One such tool, the Edinburgh Postnatal Depression Scale, has 10 questions, takes less than 5 minutes to complete, and is scored with simple arithmetic (Box 23-1). An extensive body of literature supports the validity of this tool in different cultural and socioeconomic settings. A concerning score equal to 10 or greater merits further evaluation. However, the Edinburgh Postnatal Depression Scale is considered only a screening tool, and if a patient tests positively more extensive assessment should be undertaken before presuming the presence of depression.

To prescribe paroxetine as prophylaxis in a patient who is currently asymptomatic and who does not have the diagnosis of depression would not be prudent. In some studies, the use of paroxetine has been linked with fetal cardiac anomalies. The medication should be avoided in women of reproductive age who shortly might plan other pregnancies, unless its use is demanded by clinical concerns.

All women should be assessed for mood during the postpartum period. Mood assessment by simple health care provider questioning has been repeatedly demonstrated to lack validity. In most studies that have compared health care provider questioning to structured assessment tools, the former has been shown to have an unacceptably high false-negative rate.

Referral to psychiatry or similar services is not indicated in this patient because she has no psychiatric symptoms and no psychiatric diagnosis. Should the Edinburgh Postnatal Depression Scale indicate postpartum depression, such specialized services should be considered. Practices should have a well established referral process.

Self-monitoring and report of symptoms is less than optimal for the same reasons as mood assessment by the health care provider. Patients often fail to recognize their own depressive condition until it is relatively advanced. They may attribute symptoms to situational stressors or hormones, or may simply be unwilling to acknowledge the diagnosis.

Screening for depression during and after pregnancy. Committee Opinion No. 453. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;115:394–5.

Use of psychiatric medications during pregnancy and lactation. ACOG Practice Bulletin No. 92. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008;111:1001–20.

BOX 23-1

Edinburgh Postnatal Depression Scale

Instructions for users:

1. The mother is asked to underline the response that comes closest to how she has been feeling in the previous 7 days.
2. All 10 items must be completed.
3. Care should be taken to avoid the possibility of the mother discussing her answers with others.
4. The mother should complete the scale herself, unless she has limited English or has difficulty reading.
5. The instrument may be used at 6–8 weeks to screen postnatal women. The child health clinic, postnatal check-up, or a home visit may provide suitable opportunities for its completion.

Name:_____ Address:_____ Baby's age:_____

As you recently had a baby, we would like to know how you are feeling. Please UNDERLINE the answer that comes closest to how you have felt IN THE PAST 7 DAYS, not just how you feel today.

Here is an example, already completed.

I have felt happy
- Yes, all the time
- Yes, most of the time
- No, not very often
- No, not at all

This would mean: "I have felt happy most of the time" during the past week. Please complete the other questions in the same way.

In the past 7 days:

1. I have been able to laugh and see the funny side of things
   - As much as I always could
   - Not quite as much now
   - Definitely not so much now
   - Not at all
2. I have looked forward with enjoyment to things
   - As much as I ever did
   - Rather less than I used to
   - Definitely less than I used to
   - Hardly at all

*3. I have blamed myself unnecessarily when things went wrong
   - Yes, most of the time
   - Yes, some of the time
   - Not very often
   - No, never

4. I have been anxious or worried for no good reason
   - No, not at all
   - Hardly ever
   - Yes, sometimes
   - Yes, very often

*5. I have felt scared or panicky for no very good reason
   - Yes, quite a lot
   - Yes, sometimes
   - No, not much
   - No, not at all

*6. Things have been getting on top of me
   - Yes, most of the time I haven't been able to cope at all
   - Yes, sometimes I haven't been coping as well as usual
   - No, most of the time I have coped quite well
   - No, I have been coping as well as ever

*7. I have been so unhappy that I have had difficulty sleeping
   - Yes, most of the time
   - Yes, sometimes
   - Not very often
   - No, not at all

*8. I have felt sad or miserable
   - Yes, most of the time
   - Yes, quite often
   - Not very often
   - No, not at all

*9. I have been so unhappy that I have been crying
   - Yes, most of the time
   - Yes, quite often
   - Only occasionally
   - No, not ever

*10. The thought of harming myself has occurred to me
   - Yes, quite often
   - Sometimes
   - Hardly ever
   - Never

Response categories are scored 0, 1, 2, and 3 according to increased severity of the symptom.

*Items marked with an asterisk are reverse scored (ie, 3, 2, 1, and 0). The total score is calculated by adding together the scores for each of the 10 items.

Copyright 1987 The Royal College of Psychiatrists. The Edinburgh Postnatal Depression Scale may be photocopied by individual researchers or clinicians for their own use without seeking permission from the publishers. The scale must be copied in full and all copies must acknowledge the following source: Cox JL, Holden JM, Sagovsky R. (1987) Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. British Journal of Psychiatry, 150, 782–786. Written permission must be obtained from the Royal College of Psychiatrists for copying and distribution to others or for republication (in print, online, or by any other medium). Translations of the scale, and guidance as to its use, may be found in Cox JL, Holden J. (2003) Perinatal Mental Health: A Guide to the Edinburgh Postnatal Depression Scale. London: Gaskell.

24

Preterm premature rupture of membranes

A 22-year-old woman, gravida 3, para 1, comes to the hospital at 32 3/7 weeks of gestation after leaking a large amount of fluid from the vagina. Her group B streptococcal culture was negative during an admission 3 weeks ago for preterm labor. Her vital signs are within normal limits. Membrane rupture is confirmed by pooling, nitrazine, and ferning, and her cervix appears to be closed on speculum examination. Fetal pulmonary maturity is documented on amniotic fluid testing. Fetal monitoring shows a Category I fetal heart rate tracing and no uterine contractions. Cephalic presentation is confirmed by ultrasonography. The most appropriate next step in management is to

(A) administer antenatal steroids
* (B) commence labor induction
(C) initiate antibiotics
(D) deliver at 34 weeks of gestation
(E) prescribe tocolytic medication

Preterm premature rupture of membranes (PROM) complicates 2–4% of pregnancies and accounts for approximately one third of preterm births and 20% of perinatal deaths. Risk factors for preterm PROM are similar to the risk factors associated with preterm birth in general (Appendix C). Preterm delivery, complications from oligohydramnios, and perinatal infection are important causes of perinatal morbidity and mortality. The risk of neonatal morbidity is generally a function of gestational age at membrane rupture. When premature rupture of membranes occurs before 34 weeks of gestation, the median time to delivery is approximately 1 week. Morbidities include respiratory distress syndrome, intraventricular hemorrhage, infection, necrotizing enterocolitis, pulmonary hypoplasia, skeletal deformities, cord compression, abnormal fetal testing, and a 1–2% risk of stillbirth. The risk of neurodevelopmental impairment is increased especially with intrauterine infection. Maternal complications include chorioamnionitis in approximately 30% of patients, endometritis, sepsis, and an increased risk of cesarean delivery. The risk of infection increases with decreasing gestational age at membrane rupture. Increased risks of placental abruption, cord prolapse, and retained placenta also are associated with preterm PROM.

Women with preterm PROM at 34 weeks of gestation or later should undergo delivery, although expectant management before 32 weeks of gestation is recommended. Contraindications to expectant management include intrauterine infection, cord prolapse, placental abruption, and abnormal fetal heart rate tracing. Management at 32 0/7–33 6/7 weeks of gestation is more controversial. During this time period, the risk of severe complications of prematurity is low if fetal pulmonary maturity is evident by amniotic fluid samples collected vaginally or by amniocentesis. The recommended course of action for the described patient is labor induction. If pulmonary maturity cannot be established, expectant management until 34 weeks of gestation is recommended.

Antenatal corticosteroid therapy is recommended for women with preterm PROM at 24–31 6/7 weeks of gestation because this therapy significantly reduces the risk of respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis without increasing the risks of maternal or neonatal infection. The efficacy of corticosteroid use at 32–33 completed weeks of gestation for preterm PROM is unclear based on available evidence, but treatment may be beneficial, particularly if pulmonary immaturity is documented. Regularly scheduled repeat courses of corticosteroids are not recommended and the administration of a single rescue course has not been adequately evaluated in women with preterm PROM.

The use of antibiotics is recommended during expectant management of preterm PROM at 24 0/7–33 6/7 completed weeks of gestation to prolong pregnancy and to reduce infectious and gestational age-dependent neonatal morbidity. Intravenous ampicillin and erythromycin for 2 days followed by 5 days of oral therapy decreases the likelihood of chorioamnionitis, delivery for up to 3 weeks, respiratory distress syndrome, necrotizing enterocolitis, chronic lung disease, and neonatal infectious morbidity. The use of oral erythromycin alone for 10 days decreases the rate of delivery within 48 hours, use of surfactant, and positive neonatal blood cultures. Conflicting data indicate that amoxicillin plus clavulanic acid may be associated with a significantly higher rate of necrotizing enterocolitis and, therefore, would not be recommended in this population.

The efficacy of tocolytic therapy after preterm PROM remains controversial and evidence-based recommendations cannot be made because of insufficient data. Although tocolytics may increase short-term latency, evidence documenting improved rates of perinatal morbidity or mortality is lacking.

Caughey AB, Robinson JN, Norwitz ER. Contemporary diagnosis and management of preterm premature rupture of membranes. Rev Obstet Gynecol 2008;1:11–22.

Kenyon SL, Taylor DJ, Tarnow-Mordi W. Broad-spectrum antibiotics for preterm, prelabour rupture of fetal membranes: the ORACLE I randomised trial. ORACLE Collaborative Group. [published erratum appears in Lancet 2001;358:156]. Lancet 2001;357:979–88.

Mackeen AD, Seibel-Seamon J, Grimes-Dennis J, Baxter JK, Berghella V. Tocolytics for preterm premature rupture of membranes. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD007062. DOI: 10.1002/14651858.CD007062.pub2.

Mercer BM. Is there a role for tocolytic therapy during conservative management of preterm premature rupture of the membranes? Clin Obstet Gynecol 2007;50:487–96.

Premature rupture of membranes. ACOG Practice Bulletin No. 80. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;109:1007–19.

Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database of Systematic Reviews 2006, Issue 3. Art. No.: CD004454. DOI: 10.1002/14651858.CD004454.pub2.

25

Community-acquired pneumonia

A 26-year-old multiparous woman presents with cough and fever. She resides in a shelter and has had no prenatal care. She has received no recent antibiotics and reports no chronic illness. Bedside ultrasonography suggests she is at 22 weeks of gestation. Her temperature is 38.9°C (102°F), respiratory rate is 26 breaths per minute, maternal heart rate is 110 beats per minute. Chest X-ray shows a left lower lobe infiltrate. The most appropriate initial treatment is

(A) ciprofloxacin
* (B) azithromycin
(C) ampicillin plus gentamicin
(D) oseltamivir
(E) isoniazid

Pneumonia should be suspected if a patient presents with new respiratory symptoms of cough, dyspnea, or sputum production, particularly if fever and abnormal breath sounds are also present. The presence of an infiltrate on chest X-ray confirms the diagnosis, and distinguishes pneumonia from bronchitis. During influenza season (October through March in the Northern Hemisphere), influenza also should be considered in the differential. Because the positive and negative predictive values of rapid testing for influenza are greatly affected by disease prevalence, a decision about treatment with antiviral agents (eg, oseltamivir) depends on the time of year and whether outbreaks in the community have been reported.

Pneumonia may be caused by bacteria, viruses, or fungi (Box 25-1). In community-acquired pneumonia, the organism is identified only 40–60% of the time, usually by positive blood cultures. Because *Streptococcus pneumoniae* and *Mycoplasma pneumoniae* are among the organisms most likely to be identified, coverage should be broad and should include these pathogens. Clinical signs and symptoms do not distinguish one pathogen from another.

Community-acquired pneumonia affects 1–2 in 1,000 pregnant women, similar to the attack rate among women who are not pregnant; the disease shows no predilection by trimester. Pregnant women who are hospitalized with community-acquired pneumonia are less ill than their nonpregnant counterparts, perhaps because they are less likely to progress to severe disease or because physicians are less likely to undertake outpatient management during pregnancy. Women with preexisting respiratory disease (eg, asthma) are at high risk of pneumonia, as are smokers. Diabetes mellitus, concomitant heart disease, and human immunodeficiency virus (HIV) coinfection also predispose to more severe pneumonia.

Approximately 2% of pregnant women with pneumonia require intubation and mechanical ventilation for respiratory failure. The initial assessment of a pregnant woman with suspected pneumonia should include blood cultures, as for any patient with a suspicion of sepsis, but arterial

BOX 25-1

Pathogens Isolated in Patients With Community-Acquired Pneumonia

Bacterial

Common: *Streptococcus pneumoniae, Mycoplasma pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Chlamydia pneumoniae,* and *Chlamydia psittaci*

Less common: *Pseudomonas aeruginosa, Legionella* species, *Klebsiella* species, *Moraxella catarrhalis, Bordetella pertussis, Escherichia coli, Enterobacter* species, and *Serratia* species

Viral

Common: influenza A, influenza B, and varicella-zoster virus

Less common: adenovirus species, enteroviruses (echovirus, coxsackievirus, poliovirus), Epstein-Barr virus, cytomegalovirus, respiratory syncytial virus (common in children), parainfluenza virus, human metapneumovirus, herpes simplex virus, coronaviruses, measles virus, hantavirus

Fungal

Uncommon: *Histoplasma capsulatum, Coccidioides immitis, Cryptococcus neoformans, Blastomyces hominis, Aspergillus* species, *Candida* species, Mucormycotic fungi

Other Causes

Uncommon: *Mycobacterium tuberculosis, Pneumocystis jiroveci, Toxoplasma gondii, Ascaris lumbricoides, Strongyloides stercoralis, Coxiella burnetii, Rickettsia rickettsii*

Sheffield JS, Cunningham FG. Community-acquired pneumonia in pregnancy. Obstet Gynecol 2009;114:915–22.

blood gas analysis is seldom indicated. Oxygenation can be reliably assessed in most cases by noninvasive means.

Prompt administration of appropriate antibiotics without delay is the most important principle for effective management of a woman with pneumonia. Antibiotic selection should take into account the common causes of community-acquired pneumonia, local antibiotic resistance patterns, clinical presentation, comorbid conditions, and the patient's recent antibiotic use. Initial choice of antimicrobial treatment is empiric. In the absence of comorbidities or recent antibiotic use, pregnant women can be treated with a macrolide alone (erythromycin, azithromycin, or clarithromycin). A cephalosporin should be added in all other cases. Response to therapy is indicated by defervescence and a declining white blood cell count within the first 2–4 days; resolution of radiographic and auscultatory findings may take longer. Antibiotics should not be changed in the first 72 hours unless clinical deterioration occurs or cultures dictate.

Patients may be switched to oral therapy any time they are stable hemodynamically (afebrile, normotensive, without tachypnea or tachycardia), improving clinically, and able to take medications by mouth. They may be discharged home the same day.

With older agents, a course of 10–14 days of antibiotics is commonly prescribed but newer agents have longer half-lives and, therefore, may be curative over shorter courses of therapy, eg, 5–7 days. Patients with community-acquired pneumonia should be afebrile for 48–72 hours before antibiotics are stopped.

Outpatient treatment of pneumonia is an accepted approach for adults with mild illness without comorbidities or risk factors for progression to severe disease, but it has seldom been adopted among pregnant patients. In selected antepartum patients, it appears to be safe, but a 23-hour period of hospitalized observation has been proposed before undertaking outpatient treatment.

Most pregnant women do not require tuberculosis testing unless they are at high risk of acquisition of infection or reactivation of latent tuberculosis infection. Women who reside in homeless shelters are a group at high risk of progression from latent to active disease, so a purified protein derivative test might be indicated in the described case. If a patient is deemed to be at risk of active tuberculosis, she should be isolated until she is either confirmed to be negative or treatment has proceeded to the point where she is no longer infectious. If tuberculosis is diagnosed, single-agent therapy (eg, isoniazid alone) is inadequate. Neither ciprofloxacin nor ampicillin plus gentamicin are appropriate therapy for community-acquired pneumonia.

File TM. Community-acquired pneumonia. Lancet 2003;362:1991–2001.

Goodnight WH, Soper DE. Pneumonia in pregnancy. Crit Care Med 2005;33:S390–7.

Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Infectious Diseases Society of America; American Thoracic Society; Clin Infect Dis 2007;44 Suppl 2:S27–72.

Sheffield JS, Cunningham FG. Community-acquired pneumonia in pregnancy. Obstet Gynecol 2009;114:915–22.

Yost NP, Bloom SL, Richey SD, Ramin SM, Cunningham FG. An appraisal of treatment guidelines for antepartum community-acquired pneumonia. Am J Obstet Gynecol 2000;183:131–5.

26

Positive antibody screen

A 25-year-old woman, gravida 6, para 5, comes to your office at 6 weeks of gestation for routine prenatal care. The patient's blood type is O-negative and her antibody screen result is positive. The antibody is identified as anti-Duffy (anti-Fy^a antibody). The father of the baby is Duffy antigen-negative. Her hemoglobin and hematocrit counts at 37 weeks of gestation are 9.1 g/dL and 27.8%, respectively, with a platelet count of 278,000/mm^3. On presentation to labor and delivery for an induction at 41 weeks of gestation, given the positive maternal antibody screen, the most appropriate maternal laboratory test or option is

(A) quantitate the antibody
(B) type and screen
* (C) type and crossmatch
(D) no further testing is indicated

Postpartum hemorrhage is one of the leading causes of maternal mortality. Patients with specific obstetric complications, such as placental abruption, placenta previa, and placenta accreta, are at increased risk of postpartum hemorrhage and should have blood products available for transfusion before surgery. However, patients without any risk factors may suffer from a postpartum hemorrhage, therefore, the health care provider must be prepared for the unexpected in obstetrics.

In a catastrophic hemorrhage that occurs without blood products available, O-negative red blood cells usually can be administered safely. The safety of uncrossmatched O-negative red blood cells has been well established in trauma victims. The major caveat of administering O-negative blood safely is that most individuals do not have any alloimmune antibodies. O-negative or ABO-compatible blood administered to an individual with an alloimmune antibody, such as the described patient, can cause a significant transfusion reaction. The transfusion reaction may be as severe and life threatening as ABO incompatibility.

A type and screen is ordered with prenatal laboratory tests. A type and screen identifies the ABO group, Rh type, and any major antibodies in the serum. If a major antibody is present, quantification of the antibody will help the obstetrician determine the risk of hemolytic disease in the fetus with the specific antigen. This test is useful during the antepartum period. A type and crossmatch checks for the same information as a type and screen but ensures that the patient's serum has been checked against donor red blood cells to determine compatibility. Finding compatible blood to use for a blood transfusion is more difficult and time consuming with a positive antibody screen. The difficulty increases as the frequency of the antigen in the population increases. Finding compatible blood for patients with multiple antibodies is particularly challenging and is frequently encountered in patients who require multiple blood transfusions. Therefore, on admission to the hospital, consideration should be given for type and crossmatch for any obstetric patient with a positive antibody screen.

An Rh-negative patient should not receive Rh-immune globulin if the patient is already immunized to the D antigen. However, if an Rh-negative patient has an antibody for another antigen, the patient should receive Rh-immune globulin to prevent anti-D alloimmunization.

American Red Cross. A compendium of transfusion practice guidelines. 1st ed. Washington, DC: American Red Cross; 2010. Available at: http://www.redcrossblood.org/sites/arc/files/pdf/Practice-Guidelines-Nov2010-Final.pdf. Retrieved June 10, 2010.

Brooks JP. Reengineering transfusion and cellular therapy processes hospitalwide: ensuring the safe utilization of blood products. Transfusion 2005;45:159S–71S.

Dutton RP, Shih D, Edelman BB, Hess J, Scalea TM. Safety of uncrossmatched type-O red cells for resuscitation from hemorrhagic shock. J Trauma 2005;59:1445–9.

Fuller AJ, Bucklin BA. Blood product replacement for postpartum hemorrhage. Clin Obstet Gynecol 2010;53:196–208.

Ickx BE. Fluid and blood transfusion management in obstetrics. Eur J Anaesthesiol 2010;27:1031–5.

Looney MR, Gilliss BM, Matthay MA. Pathophysiology of transfusion-related acute lung injury. Curr Opin Hematol 2010;17:418–23.

Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies; Anesthesiology 2006; 105:198–208.

27

Suppressive therapy for genital herpes

A 25-year-old pregnant woman at 38 weeks of gestation with no previous prenatal care comes to your hospital in active labor with ruptured membranes for 4 hours. She reports a history of recurrent genital herpes, noting that she feels tingling on the left labium. On inspection, a 5-mm shallow ulcer is seen. She is concerned about transmitting her infection to her child, and asks about treatment options. The best next step in management is

(A) vaginal delivery
(B) administer valacyclovir
(C) await culture results of lesion
* (D) cesarean delivery

The Centers for Disease Control and Prevention reports that herpes simplex is one of the most common sexually transmitted diseases in the United States with more than 45 million affected individuals. Data from the National Health and Nutritional Examination Survey estimate that women are twice as likely to be infected as men, and approximately 20–30% of women have evidence of past infection. Infection rates may be higher in black women. Estimates of infection in black women of up to 48% have been reported. Approximately 2% of susceptible women will develop laboratory evidence of new infection during pregnancy. Among pregnant women with a history of herpes, 75% can anticipate at least one clinical recurrence during pregnancy.

Herpes simplex virus (HSV), categorized as type 1 (HSV-1) or type 2 (HSV-2), is transmitted via direct contact to mucosa or abraded skin. After the initial infection, the virus becomes latent in the sensory ganglia. The virus can be reactivated as either recurrent ulcers or only asymptomatic shedding. Ulcerative outbreaks are categorized as a primary episode (generally more prolonged and symptomatically severe with no antibodies to either HSV-1 or HSV-2), a nonprimary first episode (antibody noted to other viral serotype than the infecting one), and a recurrent episode (same antibody serotype as the infecting virus).

No cure exists for HSV infection. Almost 100% of women infected with HSV-2 experience recurrences in the first 10 years. In general, episodes become less frequent and less severe over the years. Herpes thymidine kinase inhibitor medications, such as acyclovir and its analogues, are highly effective at shortening duration of episodes, making episodes less frequent, decreasing asymptomatic shedding, and helping to decrease risk of infection transmission to others, including sexual partners.

Acyclovir and its analogues (eg, valacyclovir) are considered safe in pregnancy and during breastfeeding, but such medications are not indicated for intrapartum use in a patient in active labor. An industry-sponsored pregnancy registry of 1,200 exposures and a prescription registry of 1,800 first-trimester exposures demonstrated no increase in neonatal anomalies. Mild, transient neonatal neutropenia can be observed after in utero acyclovir exposures.

Approximately 85% of neonatal infections occur due to contact with the virus in maternal secretions during labor or vaginal delivery. The highest risk of transmission occurs with primary infection late in pregnancy presumably because of heavy genital viral load and no transplacental antibody transmission. Recurrent herpes carries a lower risk. Table 27-1 shows risk estimates for neonatal herpes with various exposure conditions. The probability of positive culture varies among reports from 0% to 22%.

Cesarean delivery decreases but does not eliminate the risk of neonatal herpes in offspring of pregnant women with herpes genital lesions or symptoms of an impending herpes infection. Although likely more effective for prevention of transmission with intact membranes or rupture less than 4 hours, cesarean delivery may assist in avoiding transmission at any duration of rupture of

TABLE 27-1. Risk Estimates for Neonatal Herpes With Various Exposure Conditions

Clinical Condition	Probability for Positive Culture (%)	Attack Rate (%)	Neonatal Herpes Odds
Primary lesion	100	50	1:2
Genital lesion	20	2	1:250
		5	1:100
Remote lesion	2.5	5	1:800
History of herpes:	1	1	1:10,000
No lesions		5	1:1,500

Hensleigh PA. Genital herpes in pregnancy. In: Parer JT, ed. Antepartum and intrapartum management. Philadelphia (PA): Lea & Febiger; 1989. p. 108–20.

membranes. For symptomatic genital herpes infection at the time of labor, cesarean delivery remains the standard of care. Awaiting culture or polymerase chain reaction results for the patient that presents with lesions would delay cesarean delivery, which could be potentially detrimental to the fetus. Laboratory testing for asymptomatic shedding of the virus is not currently recommended.

Meta-analyses of multiple randomized clinical trials demonstrate that maternal herpes antiviral prophylaxis administered at 36 weeks of gestation until delivery can decrease the recurrence of genital herpes at delivery and, thus, the need to perform a cesarean delivery to prevent vertical transmission of herpes, and the risk of asymptomatic shedding. Direct prevention of neonatal herpes has not been demonstrated. Women with active recurrent genital herpes in pregnancy can be offered treatment with suppression for frequent recurrences. Additionally, they should be offered suppressive antiviral therapy at or beyond 36 weeks of gestation to avoid herpes indicated cesarean delivery.

Baker DA. Consequences of herpes simplex virus in pregnancy and their prevention. Curr Opin Infect Dis 2007;20:73–6.

Brown ZA, Gardella C, Wald A, Morrow RA, Corey L. Genital herpes complicating pregnancy [published errata appear in Obstet Gynecol 2006;107:428; Obstet Gynecol 2007;109:207]. Obstet Gynecol 2005;106:845–56.

Hollier LM, Wendel GD. Third trimester antiviral prophylaxis for preventing maternal genital herpes simplex virus (HSV) recurrences and neonatal infection. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD004946. DOI: 10.1002/14651858.CD004946.pub2.

Management of herpes in pregnancy. ACOG Practice Bulletin No. 82. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;109:1489–98.

Pasternak B, Hviid A. Use of acyclovir, valacyclovir, and famciclovir in the first trimester of pregnancy and the risk of birth defects. JAMA 2010;304:859–66.

Sheffield JS, Hill JB, Hollier LM, Laibl VR, Roberts SW, Sanchez PJ, et al. Valacyclovir prophylaxis to prevent recurrent herpes at delivery: a randomized clinical trial [published erratum appears in Obstet Gynecol 2006;108:695]. Obstet Gynecol 2006;108:141–7.

Sheffield JS, Hollier LM, Hill JB, Stuart GS, Wendel GD. Acyclovir prophylaxis to prevent herpes simplex virus recurrence at delivery: a systematic review. Obstet Gynecol 2003;102:1396–403.

28

Serum markers and adverse pregnancy outcome

A 29-year-old primigravid woman had a Down syndrome risk of 1:50 based on an integrated screen showing pregnancy-associated plasma protein-A (PAPP-A) of 0.3 multiples of the median (MoM), β-hCG of 1.7 MoM, alpha-fetoprotein (AFP) of 0.5 MoM, unconjugated estriol of 0.6 MoM, and inhibin A of 1.8 MoM. Amniocentesis at 17 weeks of gestation revealed a normal 46, XY karyotype. Her fundal height at 37 weeks of gestation was 34 cm and ultrasonography placed the estimated fetal weight below the 10th percentile. Her serum marker result that is most strongly associated with fetal growth restriction is

(A) β-hCG
(B) inhibin A
(C) AFP
* (D) PAPP-A
(E) unconjugated estriol

In 2007, the American College of Obstetricians and Gynecologists recommended that screening and invasive diagnostic testing for aneuploidy should be available to all women regardless of maternal age. The integrated screen couples first-trimester measurement of PAPP-A and nuchal translucency with second-trimester quadruple screen consisting of AFP, β-hCG, unconjugated estriol, and inhibin A to determine the risk of Down syndrome. The integrated screen has up to a 95% detection rate for Down syndrome with a 5% positive screen rate. Alterations in the levels of first-trimester and second-trimester serum analytes have been shown to be associated with adverse pregnancy outcomes, such as fetal growth restriction, preterm birth, preeclampsia, and pregnancy loss (Table 28-1). Of note, the analyte threshold associated with a particular adverse outcome may vary between laboratories.

Pregnancy-associated plasma protein-A is secreted by placental syncytiotrophoblasts and appears to be involved in the regulation of placental trophoblast invasion. Multiple studies have associated low PAPP-A levels with an increased risk of preeclampsia, pregnancy loss, preterm birth, and fetal growth restriction. Women with a PAPP-A level below the 5th percentile (0.42 MoM) are approximately 2.6 times more likely to deliver an infant with birth weight below the 10th percentile for gestational age.

Human chorionic gonadotropin is synthesized by syncytiotrophoblasts and functions to maintain the corpus luteum. In the first trimester, low free β-hCG levels have been associated with an increased risk of fetal growth restriction in some but not all studies. High levels of free β-hCG do not appear to be associated with an increased risk of adverse pregnancy outcome. A low or high second-trimester β-hCG level does not appear to be independently associated with fetal growth restriction.

Inhibin A, which is produced by the corpus luteum and the placenta, is associated with cell growth and immunologic recognition. An inhibin A level of 2.0 MoM or higher at 15 weeks of gestation or later is associated with an increased risk of preeclampsia, preterm birth, fetal growth restriction, and fetal demise. Low levels of inhibin A do not appear to be associated with adverse pregnancy outcome.

Alpha-fetoprotein, an oncofetal glycoprotein, is produced by the yolk sac and then the fetal liver and gastrointestinal tract. Conditions, such as placental ischemia or fetal–maternal hemorrhage, may result in increased maternal serum AFP levels with a normally developing fetus. Elevated maternal serum AFP levels are associated with an increased risk of placenta accreta, gestational hypertension, preeclampsia, placental abruption, preterm delivery, fetal growth restriction, and pregnancy loss. Levels of AFP below 0.25 MoM are associated with an increased risk of miscarriage, preterm birth, fetal demise, and macrosomia but not fetal growth restriction.

Unconjugated estriol is produced by the placenta, and levels of 0.5 MoM or less appear to be associated with an increased risk of fetal growth restriction and early pregnancy loss. Elevated levels of unconjugated estriol in the second trimester do not appear to be associated with adverse pregnancy outcome.

TABLE 28-1. Associations Between Maternal Serum Markers for Aneuploidy and Adverse Outcomes

	Preeclampsia	Birth Weight Less than 10th Percentile	Preterm Birth	Fetal Death at or Before 24 Weeks of Gestation	Fetal Death After 24 Weeks of Gestation
PAPP-A (less than 0.42 MoM)	+/++	++/+++	+ (32 weeks or less) ++ (less than 34 weeks)	++	++/+++
Free β-hCG (less than 0.21 MoM)	–	–/++	–	+++	–
AFP (more than 2.0 MoM)*	–	++	– (32 weeks or less) + (37 weeks)	+++	–/+++
hCG (more than 2.0 MoM)	–	–	–	–	– (greater than 24 weeks) +++ (greater than 500 g)
uE3 (less than 0.5 MoM)	–	+/++	–	+++	–
Inhibin A (more than 2.0 MoM)	++	+	++	–	++

Abbreviations: AFP, alpha-fetoprotein; hCG, human chorionic gonadotropin; MoM, multiples of the median; PAPP-A, pregnancy-associated plasma protein-A; uE3, unconjugated estriol. +, adjusted odds ratio (OR) greater than 1.0; ++, adjusted OR greater than 2.0; +++, adjusted OR greater than 3.0; –, adjusted OR not significant ($P \geq .05$).

*Although an isolated hCG was not significantly associated with the adverse outcomes, a hCG level greater than 2.0 MoM was significantly associated with preeclampsia, birth weight less than the 10th percentile for gestational age, preterm birth 32 weeks or less, and early and late fetal loss.

Dugoff L. First- and second-trimester maternal serum markers for aneuploidy and adverse obstetric outcomes. Society for Maternal–Fetal Medicine. Obstet Gynecol 2010;115:1052–61.

Dugoff L. First- and second-trimester maternal serum markers for aneuploidy and adverse obstetric outcomes. Society for Maternal–Fetal Medicine. Obstet Gynecol 2010;115:1052–61.

Dugoff L, Hobbins JC, Malone FD, Porter TF, Luthy D, Comstock CH, et al. First-trimester maternal serum PAPP-A and free-beta subunit human chorionic gonadotropin concentrations and nuchal translucency are associated with obstetric complications: a population-based screening study (the FASTER Trial). Am J Obstet Gynecol 2004;191:1446–51.

Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin No. 77. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;109:217–27.

Spencer K, Cowans NJ, Avgidou K, Molina F, Nicolaides KH. First-trimester biochemical markers of aneuploidy and the prediction of small-for-gestational age fetuses. Ultrasound Obstet Gynecol 2008;31:15–9.

29

Uterine inversion

A 37-year-old woman, para 7, has just given birth to a vigorous infant. The placenta is delivered after fundal massage and cord traction. Heavy uterine bleeding ensues with a mass present at the introitus consistent with uterine inversion. The best next step in pharmacologic management is to prescribe

(A) oxytocin
(B) methergine
* (C) nitroglycerin
(D) human recombinant factor VIIa
(E) 15-methyl prostaglandin $F_{2\alpha}$

Uterine inversion involves the collapse of the uterine fundus into the uterine cavity. In the case of complete inversion, a mass is present at the introitus as the fundus prolapses through the cervical os and the uterine fundus is not palpated abdominally. Although uterine inversion usually occurs after vaginal delivery, it also can happen at the time of cesarean delivery.

The most common causes of uterine inversion are excessive cord traction with a fundally implanted placenta and fundal pressure with a relaxed uterus. Uterine inversion usually presents with heavy vaginal bleeding. The fundus is not palpable and there may be maternal hemodynamic instability. It can occur before or after the delivery of the placenta. The diagnosis is made clinically at vaginal delivery; however, it is clearly evident at cesarean delivery if the uterus has been exteriorized.

The management of uterine inversion involves replacing the inverted uterus to its proper position, and at the same time rapidly treating the impending hypotension. An attempt should be made to replace the uterine fundus by pushing upward on the inverted part along the axis of the vagina. At cesarean delivery, the inverted fundus can be replaced manually by pushing up through the uterine incision.

Tocolytic agents to relax the uterus can aid in repositioning if initial attempts to reposition the uterus are unsuccessful. Nitroglycerine, terbutaline, and halogenated inhalation agents have been used for this purpose. Nitroglycerin is the preferred initial agent because of its rapid onset of action. Medications that contract the uterus, such as oxytocin, methergine, or 15-methyl prostaglandin $F_{2\alpha}$, should only be used after the uterus has been restored to its normal position to prevent recurrent inversion. Recombinant factor VIIa has been used in rare cases of massive life-threatening obstetric hemorrhage. Its serious adverse effects include intravascular clotting. Factor VIIa would never be considered first line therapy for obstetric hemorrhage.

In unusual situations, the uterus cannot be replaced manually. Laparotomy is then warranted. The Huntington procedure, which involves progressive upward traction on the inverted uterus with Babcock or Allis clamps, can be employed. If unsuccessful, an incision should be made posteriorly in the cervical ring and the inverted uterus replaced digitally followed by repair of the hysterotomy incision.

Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Obstetrical hemorrhage. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams obstetrics. 23rd ed. New York (NY): McGraw-Hill Medical Publishing Division; 2010. p. 757–803.

Gabbe SG, Niebyl JR, Simpson JL. Postpartum hemorrhage. In: Gabbe SG, Niebyl JR, Simpson JL, eds. Gabbe: obstetrics: normal and problem pregnancies. 5th ed. Postpartum hemorrhage. New York: Churchill Livingstone; 2007. p. 466–81.

Postpartum hemorrhage. ACOG Practice Bulletin No. 76. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006; 108:1039–47.

30

Ultrasonographic markers of Down syndrome

A 30-year-old woman, gravida 2, para 1, enrolls for prenatal care at 10 weeks of gestation and requests aneuploidy screening. The first-trimester ultrasonographic marker most likely to be clinically useful in screening for Down syndrome is

(A) ductus venosus velocimetry
(B) hepatic artery velocimetry
(C) nasal bone absence
* (D) nuchal translucency
(E) tricuspid regurgitation

Antenatal detection of Down syndrome remains a challenge even in the age of high-quality ultrasonographic examinations and expanded options for serum analyte testing. The high degree of phenotypic variation in fetuses with Down syndrome makes standardization of ultrasonographic markers for the syndrome difficult. In the first trimester, combinations of ultrasonography and serum tests have improved detection rates to as high as 87%. When first-trimester test results are combined with second-trimester screening options, in a variety of testing strategies, detection rates can be as high as 96%. The ultimate goal of ultrasonographic Down syndrome screening, to find a marker that confidently identifies all affected fetuses, continues to elude researchers.

Many second-trimester ultrasonographic markers have been proposed to identify Down syndrome. These so-called soft markers include echogenic bowel, echogenic intracardiac focus, nuchal thickness, renal pyelectasis, short femur, short humerus, single umbilical artery, clenched hands, clinodactyly, and sandal-gap deformity of the foot. The sensitivity and specificity of these markers alone in the detection of Down syndrome is poor. In one large prospective trial, many of the previously suspected markers were not associated with Down syndrome when identified in isolation in otherwise normal fetuses. A major abnormality routinely identifiable by ultrasonography will be present in only 25% of fetuses with Down syndrome. This finding suggests that many fetuses with Down syndrome will not be identified using soft markers alone.

First-trimester identification of a risk of Down syndrome offers the advantage of earlier genetic counseling and testing with chorionic villus sampling if available. Ultrasonographic markers of Down syndrome that have been evaluated in the first trimester include nuchal translucency, absent nasal bone, tricuspid regurgitation, crown–rump length, femur and humerus length, head and trunk volumes, hepatic artery velocimetry, ductus venosus velocimetry, and umbilical cord diameters. Of these, nuchal translucency has been the marker most evaluated in large prospective trials and in low-risk populations.

In the 1990s, an association was identified between aneuploidy and fluid that collected under the skin along the posterior fetal neck. Measurement of this hypoechoic region, now referred to as nuchal translucency measurement, was highly variable and, therefore, not reliable for Down syndrome screening in initial investigations. When the technique for measurement was standardized, including regular audits of performance, nuchal translucency measurement became a valuable tool in Down syndrome screening. Measurements require precise application of standards for the test and are generally valid between 10 4/7 weeks and 13 6/7 weeks of gestation according to the crown–rump nomogram. The Down syndrome detection rate for nuchal translucency measurement ranges between 72% and 76.8%. In combination with first-trimester serum analyte screening, the detection rate is significantly increased, depending on the strategy chosen.

Reversal of the a-wave in the ductus venosus by velocimetry and elevated peak systolic velocity in the hepatic artery, nasal bone absence, and tricuspid regurgitation have all been examined as potential first-trimester ultrasonographic markers for Down syndrome. Absence of the nasal bone and reversal of the a-wave in ductus venosus velocimetry both appear to be subject to ethnic variation. European studies of nasal bone absence in Down syndrome reported detection rates as high as 80%, but were not confirmed by studies in the United States. Elevated peak systolic velocity in the hepatic artery and the presence of tricuspid regurgitation, in addition to nasal bone absence, may be useful in patients identified as high risk after first-trimester combined screening regimens, but their use as stand-alone screening tests for Down syndrome remains under investigation.

Malone FD, Canick JA, Ball RH, Nyberg DA, Comstock CH, Bukowski R, et al. First-trimester or second-trimester screening, or both, for Down's syndrome. First- and Second-Trimester Evaluation of Risk (FASTER) Research Consortium. N Engl J Med 2005;353:2001–11.

Nicolaides KH. Screening for fetal aneuploidies at 11 to 13 weeks. Prenat Diagn 2011;31:7–15.

Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin No. 77. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;109:217–27.

Smith-Bindman R, Chu P, Goldberg JD. Second trimester prenatal ultrasound for the detection of pregnancies at increased risk of Down syndrome. Prenat Diagn 2007;27:535–44.

31

Postpartum hemorrhage

A 36-year-old woman, gravida 5, para 5, has just given birth after a precipitous labor. Thirty minutes later, the nurse reports the uterus is boggy and not responding to fundal massage. Further vigorous massage, rapid infusion of an oxytocin solution, and methylergonovine maleate administration fail to control the bleeding, which is now at approximately 1,500 cc. A second intravenous line has been started with vigorous fluid resuscitation and blood products have been ordered. Inspection of the vaginal vault and cervix reveals no lacerations, but blood is pouring from the os during the examination. Fundal exploration is negative. The placenta is inspected and found to be intact. The patient tells you that she has been experiencing bouts of dizziness. Her vital signs are the following: pulse, 130 bpm; blood pressure, 90/40 mm Hg; temperature, 37.2°C (99°F); and respiratory rate, 28 breaths per minute. In addition to transfusion, the best next step is to initiate

(A) balloon tamponade
(B) uterine artery embolization
* (C) additional uterotonics
(D) B-Lynch suture
(E) hysterectomy

Postpartum hemorrhage is both common and life threatening. The most frequent cause is atony (80%), followed by laceration and retained placenta. Risk factors for postpartum hemorrhage are listed in Box 31-1, however, postpartum hemorrhage may occur in the absence of risk factors and it should be anticipated as a possibility in any delivery. Every facility that performs obstetrics should have established protocols and drills in place in the event of postpartum hemorrhage.

Fundamental principles of postpartum hemorrhage management include the basic needs for any trauma case: two large-bore intravenous lines with exuberant crystalloid infusion, pressure on the site of bleeding (in this case, fundal massage with or without bimanual uterine compression), and rapid initiation of massive transfusion protocols. In addition, the source of the bleeding should always be investigated. Although atony is the most common source of bleeding in obstetric cases, a previously unidentified laceration or hematoma should be considered. Atony also may be secondary to a retained placental fragment and this should be excluded. However, small shreds of membrane are not likely to cause immediate massive postpartum hemorrhage.

BOX 31-1

Risk Factors for Postpartum Hemorrhage

- Prolonged labor
- Augmented labor
- Rapid labor
- History of postpartum hemorrhage
- Episiotomy, especially mediolateral
- Preeclampsia
- Overdistended uterus
- Operative delivery
- Asian or Hispanic ethnicity
- Chorioamnionitis

Data from Combs CA, Murphy EL, Laros RK Jr. Factors associated with hemorrhage in cesarean deliveries. Obstet Gynecol 1991;77:77–82 *and* Stones RW, Paterson CM, Saunders NJ. Risk factors for major obstetric haemorrhage. Eur J Obstet Gynecol Reprod Biol 1993;48:15–8.

Postpartum hemorrhage. ACOG Practice Bulletin No. 76. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006;108:1039–47.

Many techniques and devices have been developed to assist in dealing with postpartum hemorrhage, including medical, mechanical, and surgical options. Medical management includes use of an array of uterotonic agents, such as oxytocin, methylergonovine maleate, 15-methyl prostaglandin $F_{2\alpha}$, and misoprostol. These agents may be used repetitively and sequentially, although methylergonovine maleate should be avoided in patients with hypertension and 15-methyl prostaglandin $F_{2\alpha}$ should not be used in patients with asthma. Use of these pharmacologics in addition to simple uterine massage will control most atonic bleeding fairly quickly. However, in the described case, a uterotonic, such as misoprostol, usually given rectally, or 15-methyl prostaglandin $F_{2\alpha}$, administered intramuscularly, may be used. These steps can be quickly instituted while awaiting blood products and would be the appropriate next step. Attention should be paid to responsiveness. Repeat doses of uterotonics in the face of complete lack of uterine response only delays more definitive management and leads to increased blood loss.

Mechanical means starting with bimanual massage with one hand inside the vagina and the other on the fundus abdominally can be used. This technique compresses uterine musculature so that the vascular bed receives a direct "pressure dressing." An alternative mechanical option, uterine packing, is an effective option for short-term hemostasis. Because the source of the hemorrhage is the raw vascular bed created when the placenta shears away from the uterus, if muscular contractions are insufficient to compress the bleeding sinuses, an external source of pressure may be able to do so.

Packing may be accomplished with anything available including sterile lap sponges, but care should be taken to count the sponges before placement to ensure that all are removed when the packing is taken out. One way to accomplish this is to pack the sponges within a sterile glove. Another is to tie them end-to-end with the final sponge emerging outside the introitus.

For both speed and simplicity, a large balloon catheter has been developed. The device is similar to the Foley catheter except the balloon portion of the device can be filled to 500 cc. The catheter is inserted into the uterine cavity and then inflated usually from 250 cc to 300 cc with sterile saline, but no more than 500 cc is necessary to control bleeding. It is then left in place for 12–24 hours. The balloon catheter has the additional advantage over sponge packing because it can be deflated gradually in order to ensure that hemorrhage does not recur. Further, drainage from the catheter tip can be used to monitor whether significant bleeding is still occurring. Vaginal packing is frequently needed to keep the device in place. This approach also can be used as a stopgap measure before performing uterine artery embolization.

Surgical methods of hemorrhage control include uterine artery embolization, uterine artery ligation, hypogastric artery ligation, B-Lynch suture, and emergent hysterectomy. Each of these options has some distinct advantages and disadvantages. Embolization requires that skilled interventional radiologists be readily available and, thus, is not practical for many health care providers. Uterine artery ligation is quick, a skill already at hand for most obstetricians, and often very effective for lower uterine segment bleeding. A B-Lynch suture envelops and compresses the fundus providing mechanical pressure for a prolonged period (Fig. 31-1). The hypogastric artery ligation is the classic maneuver taught for the control of

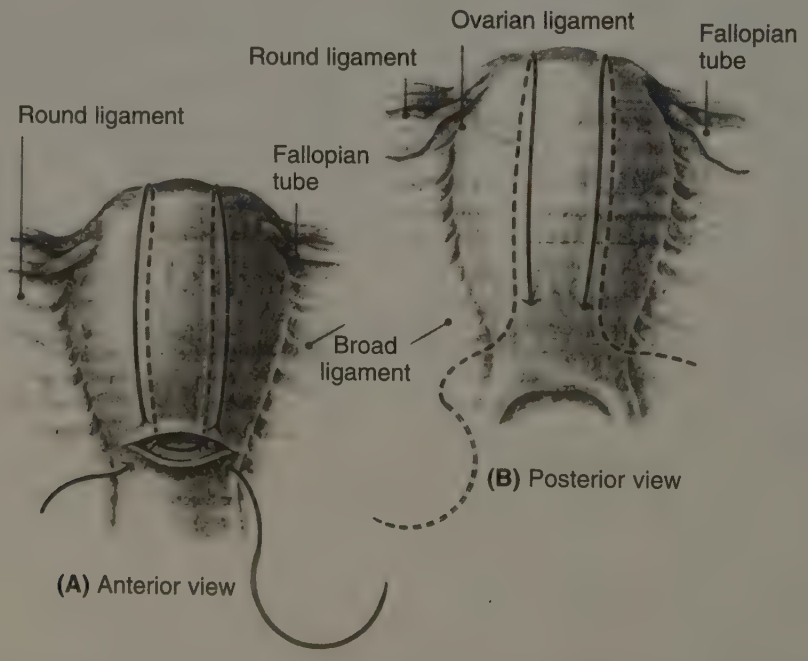


FIG. 31-1. A. Anterior view of the uterus showing the application of the B-Lynch suture. **B.** Posterior view of the uterus showing the application of the B-Lynch suture. (El-Refaey H, Rodeck C. Post-partum haemorrhage: definitions, medical and surgical management. A time for change. Br Med Bull 2003;67:205–17.)

pelvic hemorrhage, but is a somewhat more difficult skill to learn than uterine artery ligation and less practical for a novice in a high-stress situation.

All of these options allow for the preservation of further childbearing potential in a patient with a life-threatening hemorrhage. They are all extraordinarily useful and should be a part of every practicing obstetrician's armamentarium of management tools. It should be remembered that preservation of maternal life takes precedence over the attempt to preserve reproductive status. Conservative measures have shown no efficacy in a situation in which extreme blood loss has already occurred. Nothing can control hemorrhage as quickly or as definitively as a hysterectomy.

Combs CA, Murphy EL, Laros RK Jr. Factors associated with hemorrhage in cesarean deliveries. Obstet Gynecol 1991;77:77–82.

Knight M, Callaghan WM, Berg C, Alexander S, Bouvier-Colle MH, Ford JB, et al. Trends in postpartum hemorrhage in high resource countries: a review and recommendations from the International Postpartum Hemorrhage Collaborative Group. BMC Pregnancy Childbirth 2009;9:55.

Postpartum hemorrhage. ACOG Practice Bulletin No. 76. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006;108:1039–47.

Rajan PV, Wing DA. Postpartum hemorrhage: evidence-based medical interventions for prevention and treatment. Clin Obstet Gynecol 2010;53:165–81.

Stones RW, Paterson CM, Saunders NJ. Risk factors for major obstetric haemorrhage. Eur J Obstet Gynecol Reprod Biol 1993;48:15–8.

32

Diagnosis of fetal cytomegalovirus

A 32-year-old woman, gravida 3, para 2, at 22 weeks of gestation has a detailed fetal anatomic screen that reveals that her fetus has isolated bilateral cerebral ventriculomegaly. First-trimester risk assessment demonstrated a Down syndrome risk of 1:5,000 and a trisomy 18 risk of 1:10,000. Second-trimester alpha-fetoprotein (AFP) testing was 1.23 multiples of the median. There is no family history of ventriculomegaly. The toxoplasma serology result is negative, but cytomegalovirus (CMV) serology returns positive immunoglobulin G (IgG) and immunoglobulin M (IgM). The most sensitive and specific test for diagnosing fetal CMV infection is

(A) repeat CMV serology
(B) CMV IgG avidity testing
* (C) amniocentesis for CMV DNA polymerase chain reaction
(D) fetal magnetic resonance imaging
(E) cordocentesis for fetal liver function tests

Cytomegalovirus is a double-stranded DNA herpesvirus that infects approximately 50–85% of adults in the United States by age 40 years. Seroconversion occurs in approximately 2–2.5% of pregnancies and intrauterine infection complicates 0.5–2% of all live births. The most common viral cause of cerebral palsy is CMV, and it is the most common infectious cause of fetal deaths. In primary maternal infections, the transmission risk is approximately 40%. More infants acquire CMV from recurrent (nonprimary) maternal infections, which have only a 1% vertical transmission risk. Fetal and neonatal manifestations are usually less severe in nonprimary infections. Accordingly, there is a high prevalence of latent maternal CMV, and maternal antibodies do not necessarily prevent vertical transmission. These realities complicate CMV screening.

Routine serologic testing or screening for CMV in patients who are asymptomatic during pregnancy is not recommended. Maternal IgM antibody screening is limited for differentiating primary from recurrent infection because IgM antibodies can persist, which makes it difficult to use such results in counseling patients. In addition, maternal immunity with IgG antibodies does not eliminate the possibility of fetal infection. The typical transmission route for CMV is through body fluids (eg, saliva, urine, and feces). Therefore, hand washing is a critical preventive measure, particularly for health care workers and people who care for young children.

Clinical signs of maternal infection include an influenza-like illness, elevated transaminases, and lymphocytosis. These clinical signs rarely are helpful for diagnosis. Viral culture of the patient's urine or throat may be performed during the symptomatic phase; however, serology is most commonly used for diagnosis. An initial enzyme-linked immunosorbent assay (ELISA) serology test should be followed by a repeat ELISA serology test

2 weeks later. A fourfold increase in IgG over paired tests or an IgM level 30% greater than the IgG level can be used for confirming maternal acute infection. For fetal diagnosis, amniotic fluid retrieved by amniocentesis may be sent for CMV DNA polymerase chain reaction, which has a sensitivity of 95% if performed at or beyond 21 weeks of gestation. Because the sensitivity decreases to 65%, most experts recommend repeat testing of the amniotic fluid after at least 6 weeks before 21 weeks of gestation. Cordocentesis for fetal studies is rarely done because of the specialized nature of the procedure and the good performance of amniotic fluid studies.

Many health care providers may order CMV avidity tests to determine the timing of maternal infection. A CMV avidity test measures the length of exposure to the antigen, with avidity improving with duration of exposure. Thus, low avidity indicates early exposure and high avidity suggests prolonged exposure consistent with resolved or latent infection. Although these tests may be helpful to assess timing of maternal infection, they do not specifically address the question of fetal infection.

Ultrasonographic findings (including cerebral ventriculomegaly, microcephaly, echogenic bowel, hepatosplenomegaly, ascites, intracranial calcifications, and intrauterine growth restriction) can aid in the diagnosis of fetal infection and are often the signs that initiate maternal serum testing. Fetal magnetic resonance imaging is useful in further assessing intracranial anomalies, such as ventriculomegaly, although it has no utility in the diagnosis of infection. Approximately 90% of infants with congenital CMV do not show signs on ultrasonography; 0.5–15% of these infants are at risk of neonatal sequelae. Of those that do show signs on ultrasonography, 50% are at risk of cytomegalic inclusion disease—jaundice, hepatosplenomegaly, petechial rash, multiorgan involvement (especially central nervous system anomalies)—and 80% are at risk of late complications, including hearing–vision impairment, mental retardation, cerebral palsy, and developmental–cognitive delays.

Management of perinatal CMV transmission relies heavily on prevention. Treatments for CMV are typically limited to serious maternal manifestations or immunocompromised hosts. Intravenous hyperimmune globulin administration, to produce passive immunity, shows promise as a potential therapy in the future, but should be considered experimental until clinical trials prove it to be beneficial.

American College of Obstetricians and Gynecologists. Perinatal viral and parasitic infections. ACOG Practice Bulletin 20. Washington, DC: ACOG; 2000.

Centers for Disease Control and Prevention. Cytomegalovirus (CMV) and congenital CMV infection. Atlanta (GA): CDC; 2010. Available at: http://www.cdc.gov/cmv/index.html. Retrieved June 11, 2012.

Duff P. A thoughtful algorithm for the accurate diagnosis of primary CMV infection in pregnancy. Am J Obstet Gynecol 2007;196:196–7.

Fowler KB, Stagno S, Pass RF. Maternal immunity and prevention of congenital cytomegalovirus infection. JAMA 2003;289:1008–11.

Fowler KB, Stagno S, Pass RF, Britt WJ, Boll TJ, Alford CA. The outcome of congenital cytomegalovirus infection in relation to maternal antibody status. N Engl J Med 1992;326:663–7.

Liesnard C, Donner C, Brancart F, Gosselin F, Delforge ML, Rodesch F. Prenatal diagnosis of congenital cytomegalovirus infection: prospective study of 237 pregnancies at risk. Obstet Gynecol 2000;95:881–8.

Nigro G, Mazzocco M, Anceschi MM, La Torre R, Antonelli G, Cosmi EV. Prenatal diagnosis of fetal cytomegalovirus infection after primary or recurrent maternal infection. Obstet Gynecol 1999;94:909–14.

33

Anemia workup

A 42-year-old white woman, gravida 1, comes to your office for her first prenatal visit at 12 weeks of gestation. She has no personal or family history of anemia. She is a vegan. Her prenatal laboratory results show a white blood count of 10,200/mm^3, hemoglobin level 8.5 g/dL, hematocrit level 26.5%, and platelet count of 247,000/mm^3. The mean corpuscular volume is 73 fL. Her serum ferritin level is 6 micrograms/L and her iron level is 23 micrograms/L. The best next step in her management is

(A) hemoglobin electrophoresis
(B) vitamin B_{12} supplementation
(C) erythropoietin injections
* (D) iron supplementation
(E) folate supplementation

The definition of *anemia* in females is a hemoglobin level of 11.0 g/dL and a hematocrit level of less than 33%. The definition is the same in the first trimester and third trimester of pregnancy but it changes in the second trimester to a hemoglobin level of 10.5 g/dL and a hematocrit level of 32%. Mean corpuscular volume is classified as follows: microcytic (less than 80 fL), normocytic (81–99 fL), or macrocytic (greater than 100 fL). The most common cause of microcytic anemia is iron deficiency. Other causes of microcytic anemia include thalassemias especially in specific ethnic groups, chronic disease, sideroblastic anemia, copper deficiency, and lead poisoning. The most common cause of macrocytic anemia is lack of vitamin B_{12}, folate, or a combination of the two. Vegans do not eat meat or any product from an animal, such as milk or eggs. This diet is deficient in B_{12} and is low in folate. Alcoholics are at increased risk of macrocytic anemia due to folate deficiency, vitamin B_{12} deficiency, or a combined deficiency of the two. Some medications, eg, zidovudine and long-term use of H_2 blockers and proton pump inhibitors, predispose patients to macrocytic anemia.

Females are at risk of iron-deficient anemia due to menstrual cycles, short interval pregnancies, and diets poor in iron-rich food. The diagnosis of iron-deficient anemia is made by a complete blood count and evaluation of the red blood cell indices. Table 33-1 compares the laboratory characteristics of iron-deficient anemia and thalassemia. Measurement of ferritin levels has the highest sensitivity and specificity for diagnosing iron-deficient anemia. Treatment of iron-deficient anemia is typically oral iron supplementation. In refractory cases, parenteral therapy may be indicated.

A detailed history is indicated in any patient with anemia. Patients also can develop gastrointestinal conditions, such as intestinal polyps, colon cancer, and hemangioma that can result in iron-deficient anemia from chronic blood loss. Anyone with gastrointestinal symptoms should be evaluated for occult blood loss. Although the best test for occult blood is debatable, a positive test result requires a further evaluation of the gastrointestinal tract.

Thalassemia should be suspected in microcytic anemia if serum iron levels are normal. Individuals of African, Southeast Asian, and Mediterranean descent are at a higher risk of thalassemia than other ethnic groups. Beta-thalassemia can be diagnosed with a hemoglobin electrophoresis but alpha-thalassemia requires specific molecular testing.

Erythropoietin is a glycoprotein produced primarily by the kidneys that promotes red blood cell production in the bone marrow. Erythropoietin levels are elevated during pregnancy in the second trimester and third trimester. Therapy with erythropoietin is not warranted in a healthy

TABLE 33-1. Laboratory Characteristics of Iron-Deficient Anemia Compared With Thalassemia

Laboratory Test	Iron-Deficient Anemia	Thalassemia
Plasma iron level	Decreased	Normal
Plasma total iron-binding capacity	Increased	Normal
Transferrin saturation	Decreased	Normal
Serum ferritin level	Decreased	Normal
Free erythrocyte level protoporphyrin	Increased	Normal

Modified from anemia in pregnancy. ACOG Practice Bulletin No. 95. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008;112:201–7.

pregnant woman but may be beneficial during pregnancy in women with end-stage renal disease.

Anemia in pregnancy. ACOG Practice Bulletin No. 95. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008; 112:201–7.

Joint World Health Organization/Centers for Disease Control and Prevention. Technical consultation on the assessment of iron status at the population level. Geneva, Switzerland: World Health Organization; 2004.

Stoltzfus R, Dreyfuss M. Guidelines for the use of iron supplements to prevent and treat iron deficiency anemia. Washington, DC: ILSI Press; 1998.

34

Statins and drug exposure during pregnancy

You are consulted by a 40-year-old woman with type 2 diabetes mellitus, hypertension, and hyperlipidemia, who has a positive pregnancy test result. Her current medications include metformin, amlodipine, and simvastatin. She is concerned about medication exposure to her fetus. Of the medications that she is taking, you recommend discontinuation of

(A) none
(B) metformin
(C) amlodipine
* (D) simvastatin

Treatment of diabetes mellitus should continue during pregnancy. Glucose control is crucial because of the known risks of hyperglycemia to the fetus. Both glyburide and metformin have been used successfully during pregnancy, and are not believed to be teratogenic. Because metformin is used in polycystic ovary syndrome as a treatment for subfertility, it is commonly given early in pregnancy even to women who do not have diabetes mellitus.

Little consensus exists on the treatment of chronic hypertension during pregnancy. Women with mild or moderate chronic hypertension may not require antihypertensive therapy during pregnancy in the absence of comorbidities, and there is some concern that antihypertensive therapy may affect uteroplacental blood flow or fetal growth. In the described patient, however, diabetes is a comorbid condition, and hypertension is known to contribute to the development of diabetic kidney disease; thus, continuing antihypertensive therapy is prudent.

The choice of drug may be difficult, as the first-line agent for hypertension in diabetes is often an angiotensin-converting enzyme (ACE) inhibitor, which is contraindicated in pregnancy. In the first trimester, use of ACE inhibitors has been, albeit inconsistently, associated with congenital anomalies. In the second trimester and third trimester, use of ACE inhibitors has been associated with oligohydramnios, fetal–neonatal renal failure, closure of the ductus arteriosus, and death. Another drug frequently used for hypertension in diabetes is amlodipine, which, like nifedipine, is a dihydropyridine calcium-channel blocker, although longer-acting. The calcium-channel blockers are not considered to be teratogenic during pregnancy, although there may be an increased risk of neonatal seizures.

Statins are widely used both for the treatment of cardiovascular disease and for primary prevention of stroke, myocardial infarction, and mortality among individuals with risk factors. Limited human data exist for the use of statins in pregnancy. The theoretical argument against the use of statins, which are 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors, is that they may interfere with cholesterol pathways in the developing embryo. Early data from the manufacturer suggested increased risk of anomalies with exposure to simvastatin and lovastatin during pregnancy, and some case series report central nervous system, facial, and limb abnormalities. Other case series, however, report no additional risk of congenital anomalies with pregnancy exposure to statins. No controlled trials are available, and the total number of exposures is not high. The U.S. Food and Drug Administration currently lists simvastatin and related drugs as category X, ie, drugs considered to be contraindicated in pregnant women.

No maternal benefit has been ascertained in continuing treatment with statins during pregnancy. In most cases, it seems to be safe to interrupt treatment for hyperlipidemia. The role of statins in primary prevention of cardiovascular events is less well established than their role after devel-

opment of coronary heart disease. If this cannot safely be done, consideration should be given to switching from a lipophilic to a hydrophilic statin, such as pravastatin, which is less distributed into embryonic tissues. In contrast, interruption of treatment for diabetes mellitus or for hypertension may compromise maternal health.

The most prudent course of action would be to stop the patient's simvastatin and to continue to treat her hypertension and diabetes mellitus. The patient should be counseled as to the risks and benefits of drugs to which she has been exposed during pregnancy, the background risk of anomalies, and the ability of prenatal ultrasonography to detect some anomalies. General teratology principles hold that the period of greatest risk is during the first trimester. Counseling about medication exposure during pregnancy varies with the gestational age at which exposure occurs. In addition, the risk–benefit ratio must be considered when prescribing in pregnancy: maternal benefit from a given drug (or maternal risk if the drug is discontinued) may override the potential fetal risks. In counseling a patient about drug exposures during pregnancy, it is important to note that the background risk of birth defects in an unselected population is approximately 2–3%.

Davis RL, Eastman D, McPhillips H, Raebel MA, Andrade SE, Smith D, et al. Risks of congenital malformations and perinatal events among infants exposed to calcium channel and beta-blockers during pregnancy. Pharmacoepidemiol Drug Saf 2011;20:138–45.

Edison RJ, Muenke M. Mechanistic and epidemiologic considerations in the evaluation of adverse birth outcomes following gestational exposure to statins. Am J Med Genet A 2004;131:287–98.

Manson JM, Freyssinges C, Ducrocq MB, Stephenson WP. Postmarketing surveillance of lovastatin and simvastatin exposure during pregnancy. Reprod Toxicol 1996;10:439–46.

Ofori B, Rey E, Berard A. Risk of congenital anomalies in pregnant users of statin drugs. Br J Clin Pharmacol 2007;64:496–509.

Petersen EE, Mitchell AA, Carey JC, Werler MM, Louik C, Rasmussen SA, et al. Maternal exposure to statins and risk for birth defects: a case-series approach. Am J Med Genet A 2008;146A:2701–5.

Pollack PS, Shields KE, Burnett DM, Osborne MJ, Cunningham ML, Stepanavage ME. Pregnancy outcomes after maternal exposure to simvastatin and lovastatin. Birth Defects Res A Clin Mol Teratol 2005;73:888–96.

Pregestational diabetes mellitus. ACOG Practice Bulletin No. 60. American College of Obstetricians and Gynecologists. Obstet Gynecol 2005;105:675–85.

Quan A. Fetopathy associated with exposure to angiotensin converting enzyme inhibitors and angiotensin receptor antagonists. Early Hum Dev 2006;82:23–8.

Taguchi N, Rubin ET, Hosokawa A, Choi J, Ying AY, Moretti ME, et al. Prenatal exposure to HMG-CoA reductase inhibitors: effects on fetal and neonatal outcomes. Reprod Toxicol 2008;26:175–7.

35

Gestational diabetes mellitus

A 36-year-old woman, gravida 2, para 1, returns to your clinic at 24 weeks of gestation for a prenatal care visit. She wants to be sure that she does not have diabetes mellitus during her pregnancy. The most accepted method for screening for gestational diabetes mellitus in the United States is

(A) hemoglobin A_{1C}
(B) fasting blood glucose
* (C) 50-g glucose challenge test
(D) urine glucose level
(E) 2-hour, 75-g glucose challenge test

Gestational diabetes mellitus is defined as carbohydrate intolerance that begins or is first recognized during pregnancy. Demographic identifiers and features from the medical history are known to be associated with a higher risk of gestational diabetes mellitus and are similar to risk factors for type 2 diabetes mellitus. Use of history alone to identify at-risk women, such as a history of a large baby, will miss up to 50% of women with glucose intolerance in pregnancy identified by glucose testing.

Debate exists about routine universal screening for gestational diabetes. Diagnostic criteria in the United States were based on development of subsequent type 2 diabetes mellitus and not pregnancy outcome. The U.S. Preventive Services Task Force recommends screening only for high-risk groups in pregnancy. Large international trials have demonstrated benefit for pregnancy outcomes through identification and treatment of mild gestational hyperglycemia. Decreases in maternal preeclampsia, macrosomia, neonatal metabolic problems, and composite adverse outcomes in trials suggest that there may be benefit to identification of women with milder degrees of glucose intolerance.

The American Diabetes Association recommends risk assessment for gestational diabetes at the first prenatal

visit with testing for individuals at high risk (ie, personal history of gestational diabetes, marked obesity, glycosuria, strong family history) as soon as feasible. If the test result is negative, the patient should be retested at 24–28 weeks of gestation.

For women at low risk of development of gestational diabetes (ie, age less than 25 years, normal weight, low-risk ethnic group, no diabetes in first-degree relatives, no personal history of abnormal glucose tolerance, no poor obstetric outcome), no glucose testing is necessary. For some areas of the United States, this excludes so few women that universal testing is used.

For average-risk women, the test usually is performed at 24–28 weeks of gestation. Timing is based on a balance between the onset of third-trimester physiologic changes that affect glucose metabolism and allowance of adequate time to manage glucose intolerance.

In the United States, a two-step approach is generally used with a preliminary 1-hour 50-g glucose screening test followed by a diagnostic 3-hour, 100-g glucose tolerance test for those who exceed the threshold for the initial screen. See Table 35-1 for diagnostic criteria for gestational diabetes mellitus. Outside the United States, a one-step 2-hour, 75-g test generally is used. The American College of Obstetricians and Gynecologists does not recommend the one-step 2-hour, 75-g test because clinical trial data are not available for this screening strategy in the United States, and the expectation is that with this test a larger number of patients would be classified as having gestational diabetes mellitus.

For the 1-hour 50-g test, varying cutoffs have been used. The cutoff of 140 mg/dL (7.8 mmol/L) is 80% sensitive for an abnormal diagnostic test result and 130 mg/dL (7.2 mmol/L) is 90% sensitive for an abnormal diagnostic test result. Likewise, varying cutoffs have been used for the 3-hour, 100-g diagnostic test.

Elevated fasting glucose levels are highly specific for the diagnosis of diabetes, but screening fasting glucose measurements lack sensitivity for lesser degrees of glucose intolerance that might be clinically significant. Likewise, elevation in hemoglobin A_{1C} is highly specific for the diagnosis of diabetes but lacks sensitivity. Urine glycosuria is neither adequately sensitive nor specific for the diagnosis of glucose intolerance in pregnancy, although persistent high levels of glycosuria might prompt further evaluation.

Ingestion of high concentration glucose drinks for diagnostic purposes can be problematic for women with pregnancy-associated nausea. The fat and protein in a high carbohydrate mixed meal or a candy bar blunts absorption of glucose and requires a low cutoff for screening, which makes this approach insensitive. Candy that consists mostly of simple sugars, like jelly beans, has been substituted but the quantity to be ingested makes this option only slightly more palatable than diagnostic drinks and, thus, lacks sensitivity.

Diagnosis and classification of diabetes mellitus. American Diabetes Association. Diabetes Care 2012;35 Suppl 1:S64–71.

Gestational diabetes mellitus. American Diabetes Association. Diabetes Care 2004;27 Suppl 1:S88–90.

Gestational diabetes mellitus. American Diabetes Association. Diabetes Care 2003;26 Suppl 1:S103–5.

Hillier TA, Vesco KK, Pedula KL, Beil TL, Whitlock EP, Pettitt DJ. Screening for gestational diabetes mellitus: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med 2008;148: 766–75.

Landon MB. Is there a benefit to the treatment of mild gestational diabetes mellitus? Am J Obstet Gynecol 2010;202:649–53.

Screening and diagnosis of gestational diabetes mellitus. Committee Opinion No. 504. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:751–3.

Tieu J, Middleton P, McPhee AJ, Crowther CA. Screening and subsequent management for gestational diabetes for improving maternal and infant health. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD007222. DOI: 10.1002/14651858.CD007222.pub2.

TABLE 35-1. Diagnostic Criteria for the 100-g, 3-Hour Tolerance Test for Gestational Diabetes Mellitus*

	Plasma or Serum Glucose Level Carpenter and Coustan Conversion		Plasma Level National Diabetes Data Group Conversion	
Status	**mg/dL**	**mmol/L**	**mg/dL**	**mmol/L**
Fasting	95	5.3	105	5.8
1 Hour	180	10.0	190	10.6
2 Hours	155	8.6	165	9.2
3 Hours	140	7.8	145	8.0

*A positive diagnosis requires that two or more thresholds be met or exceeded.

Screening and diagnosis of gestational diabetes mellitus. Committee Opinion No. 504. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:751–3.

36

Decreased fetal movement

A 21-year-old woman, gravida 1, is seen at 37 weeks of gestation with a subjective report of diminished fetal movement over the past 18 hours. Her fundal height is consistent with gestational dates. Fetal heart rate is auscultated at 140 beats per minute and fetal movement is palpable. She had a benign prenatal course except for a 1-hour, 151-mg/dL glucose screen at 28 weeks of gestation, followed by a normal 3-hour oral glucose tolerance test. A modified biophysical profile revealed a reactive nonstress test and an amniotic fluid index of 12 cm. The most appropriate next step in her management is

(A) twice weekly nonstress tests
(B) once weekly biophysical profile
(C) induction of labor
* (D) reassurance

Third-trimester reports of diminished fetal movement are common. The perception of diminished movement is due to the increasing size of the growing fetus and the inability of the fetus to produce vigorous kicking. The described assessment, especially the reactive nonstress test, is reassuring and makes the likelihood of intrauterine fetal demise unlikely. Given the reactive nonstress test, the risk of an unexplained stillbirth in the next week would be less than 1–2 per 1,000 fetuses. The best next step in her management would be reassurance.

Different clinical regimens for fetal movement assessment include "count to ten" or at least four movements per hour. These techniques have not been compared directly in a randomized trial. Daily fetal movement counts can enable detection of deterioration in fetal status. Labor induction or additional antepartum testing generally is not indicated in an uncomplicated pregnancy in the presence of normal fetal movement.

Some health care providers choose to universally recommend fetal movement assessment in the absence of complaints such as self-reported diminution in movement. Large randomized trials have failed to demonstrate improvements in perinatal outcomes when fetal movement assessment is used as a routine strategy. Many self-help books and web sites advise patients to practice these techniques. It also is helpful if obstetricians have a practical plan for women who sense diminished fetal activity.

In addition to the increased likelihood of cesarean delivery that induction of labor poses for a pregnant woman with an unfavorable cervix, delivery before 39 completed weeks of gestation appears to be associated with greater risks of neonatal complications. Subjective report of diminished activity should be confirmed by evidence of fetal compromise.

Froen JF, Heazell AE, Tveit JV, Saastad E, Fretts RC, Flenady V. Fetal movement assessment. Semin Perinatol 2008;32:243–6.

Froen JF, Tveit JV, Saastad E, Bordahl PE, Stray-Pedersen B, Heazell AE, et al. Management of decreased fetal movements. Semin Perinatol 2008;32:307–11.

Haws RA, Yakoob MY, Soomro T, Menezes EV, Darmstadt GL, Bhutta ZA. Reducing stillbirths: screening and monitoring during pregnancy and labour. BMC Pregnancy Childbirth 2009;9 Suppl 1:S5.

Hijazi ZR, East CE. Factors affecting maternal perception of fetal movement. Obstet Gynecol Surv 2009;64:489,97; quiz 499.

Hoffmire CA, Chess PR, Ben Saad T, Glantz JC. Elective delivery before 39 weeks: the risk of infant admission to the neonatal intensive care unit. Matern Child Health J 2012;16:1053–62.

37

Intrahepatic cholestasis of pregnancy

A 38-year-old woman, gravida 4, para 2, is seen at 29 weeks of gestation for generalized intense itching for the past week. The itching is worst on her hands and feet. She does not report any infectious contacts or new skin care products. Her temperature is 37.0°C (98.6°F), blood pressure is 135/85 mm Hg, and pulse is 90 beats per minute. She appears in no acute distress. Her sclerae are nonicteric and her oropharynx is normal. She has no rash. Her cervix is closed and long. The fetal heart rate is 135 beats per minute and reassuring. Urine dipstick test result is negative for protein. Laboratory evaluation reveals her white blood count is 9.0×10^9/L, hematocrit is 33%, and platelet count is 240,000/mm^3. Metabolic panel shows the serum alanine transaminase level is 55 units/L and the total bilirubin level is 0.7 mg/dL. The most appropriate diagnostic test is

(A) serum alkaline phosphatase
(B) serum ammonia
* (C) serum bile acid levels
(D) serum glucose

Intrahepatic cholestasis of pregnancy is defined as pregnancy-related pruritus with abnormal liver function that resolves after delivery in the absence of other acute liver disease. Although skin findings are typically limited to excoriations due to scratching, intrahepatic cholestasis of pregnancy-associated pruritus is usually intense and centered on the palms of the hands and soles of the feet. The condition is associated with adverse fetal outcomes, although the exact rates of fetal complication are not known. Risks of intrahepatic cholestasis of pregnancy include preterm labor, meconium staining of the amniotic fluid, abnormal fetal heart tracings, and intrauterine fetal demise. The time of greatest risk to the fetus for demise appears to be between 37 weeks and 39 weeks of gestation. The etiology of the disease is thought to be due to pregnancy-associated hormone levels that inhibit bile acid transport in patients who are genetically susceptible. The incidence varies depending on geographic location and other environmental factors. High rates are seen in South America, especially in Chile, and during the winter in Finland, Sweden, and Portugal. It has also been found that intrahepatic cholestasis of pregnancy rates are increased in twin pregnancies and after in vitro fertilization.

Measurement of serum bile acid levels is the most appropriate test to diagnose intrahepatic cholestasis of pregnancy. Total bile acid levels in normal pregnancy are typically less than 10–14 mmol/L. *Mild intrahepatic cholestasis of pregnancy* is defined as a bile acid level of approximately 14 mmol/L. Total bile acid levels of more than 40 mmol/L are associated with risk of fetal loss. For early diagnosis, either cholic acid or the ratio of cholic acid to chenodeoxycholic acid are recommended. Cholic acid levels may remain constant or increase in the third trimester, but should remain in the normal range (less than 1.5 mmol/L) in patients without intrahepatic cholestasis of pregnancy. The reported normal range for the cholic acid to chenodeoxycholic acid ratio is 0.68 to 1.9 at term. As in the described patient, serum transaminase levels may be normal, or may be elevated up to 10-fold. Bilirubin values are typically normal.

Urine studies in patients with intrahepatic cholestasis of pregnancy will demonstrate increased total bile acid excretion, but normal proteinuria levels are unchanged. Alkaline phosphatase can increase in patients with intrahepatic cholestasis of pregnancy, but it also is made in large quantities by the placenta and, therefore, will not be helpful. Serum ammonia levels are unaffected by the disease but often found to be elevated in acute fatty liver of pregnancy. Impaired glucose tolerance in patients with intrahepatic cholestasis of pregnancy has been shown in one study, but fasting glucose levels were no different than in controls.

Commonly recommended management for intrahepatic cholestasis of pregnancy includes treatment with ursodeoxycholic acid and delivery at or near term. Because laboratory results for intrahepatic cholestasis of pregnancy testing may be delayed by up to 1 week, it may be necessary to begin management before confirmatory evidence is available. Symptomatic relief of pruritus may be difficult to achieve, but antihistamines are a common approach. Although antepartum surveillance does not perform well in preventing intrahepatic cholestasis of pregnancy-associated deaths, it is an important part of management in these patients. Delivery at or near term is thought to preempt the risk for intrauterine fetal demise. No association has been observed between ursodeoxycholic acid and known fetal or maternal complications,

and it can produce relief of pruritus and resolution of bile acid level abnormalities within 7 days of treatment initiation. Neither pharmacotherapy nor induction of labor has been tested in randomized trials. Ongoing genetic research into susceptible populations suggests that patients with mutations in the *MDR3 (ABCB4)* gene, which encodes a phospholipid transport protein, may account for 15% of cases of intrahepatic cholestasis of pregnancy. Patients with the *MDR3* mutation also may be at risk of serious liver disease later in life.

Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. World J Gastroenterol 2009;15:2049–66.

Hardikar W, Kansal S, Oude Elferink RP, Angus P. Intrahepatic cholestasis of pregnancy: when should you look further? World J Gastroenterol 2009;15:1126–9.

Lee NM, Brady CW. Liver disease in pregnancy. World J Gastroenterol 2009;15:897–906.

Mays JK. The active management of intrahepatic cholestasis of pregnancy. Curr Opin Obstet Gynecol 2010;22:100–3.

38

Thrombocytopenia

A 26-year-old primigravid woman at 36 weeks of gestation has a platelet count of 62,000/mm^3 noted on routine blood work. She does not have a history of thrombocytopenia, easy bruising, menorrhagia, rash, or joint ache. She has a history of Raynaud phenomenon and chronic hypertension. Her only medication is prenatal vitamins. Her first-trimester laboratory results include a negative human immunodeficiency virus (HIV) test and a platelet count of 104,000/mm^3. Her blood pressure is 138/86 mm Hg and she has trace protein in her urine. Her hemoglobin and transaminase levels are normal. Physical examination is significant for mild pedal edema. The diagnosis that most likely explains her thrombocytopenia is

(A) gestational thrombocytopenia
* (B) immune thrombocytopenic purpura
(C) preeclampsia
(D) systemic lupus erythematosus

Thrombocytopenia complicates 5–10% of pregnancies and may be secondary to any one of a number of conditions (Box 38-1). The platelet count decreases by approximately 10% during pregnancy, particularly in the third trimester, but remains within normal limits. *Thrombocytopenia* generally is defined as a platelet count less than 150,000/mm^3. *Mild thrombocytopenia, moderate thrombocytopenia,* and *severe thrombocytopenia* are defined as a platelet count of 100,000–150,000/mm^3, 50,000–100,000/mm^3, and less than 50,000/mm^3, respectively. Clinically significant bleeding usually is limited to patients with a platelet count less than 20,000/mm^3, although excessive bleeding associated with trauma or surgery is uncommon in patients with a platelet count greater than 50,000/mm^3. Thrombocytopenia is due to increased platelet destruction (the most common cause in pregnancy) or decreased platelet production.

Immune thrombocytopenic purpura, a diagnosis of exclusion, accounts for 5% of pregnancy-associated thrombocytopenia cases and is characterized by immunologically mediated platelet destruction by immunoglobulin G antiplatelet antibodies that recognize platelet membrane glycoproteins. Women with immune thrombocytopenic purpura generally have a history of thrombocytopenia and easy bruising, petechiae, or bleeding that predates pregnancy, but some women are completely asymptomatic. The presence of first-trimester thrombocytopenia in the patient described is most consistent with a diagnosis of immune thrombocytopenic purpura. The course of the disease usually is not affected by pregnancy, although there are variable reports of exacerbation during pregnancy. The primary risk to the mother is hemorrhage during the peripartum period due to severe thrombocytopenia. Maternal immunoglobulin G antiplatelet antibodies can cross the placenta leading to severe neonatal thrombocytopenia in 9–15% of patients, serious bleeding complications in approximately 3% of patients, and intracranial hemorrhage in less than 1% of neonates. Hemorrhagic complications associated with neonatal thrombocytopenia are unrelated to mode of delivery. Therefore, fetal platelet

BOX 38-1

Causes of Thrombocytopenia in Pregnancy

- Gestational thrombocytopenia
- Pregnancy-induced hypertension
- Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome
- Pseudothrombocytopenia (laboratory artifact)
- Human immunodeficiency virus (HIV) infection
- Immune thrombocytopenic purpura
- Systemic lupus erythematosus
- Antiphospholipid syndrome
- Hypersplenism
- Disseminated intravascular coagulation
- Thrombotic thrombocytopenic purpura
- Hemolytic uremic syndrome
- Congenital thrombocytopenias
- Medications (eg, heparin, quinine, quinidine, zidovudine, or sulfonamides)

American College of Obstetricians and Gynecologists. Thrombocytopenia in pregnancy. ACOG Practice Bulletin 6. Washington, DC: ACOG; 1999.

count determination is unnecessary. Cesarean delivery is reserved for the usual obstetric indications in women with immune thrombocytopenic purpura.

Gestational thrombocytopenia, which typically occurs in the third trimester, affects 5–8% of pregnancies and accounts for 70% of cases of thrombocytopenia in pregnancy. Women with this condition are asymptomatic and have no history of thrombocytopenia before pregnancy. A platelet count between 130,000/mm^3 and 150,000/mm^3 is seen in 70% of patients; a platelet count below 70,000/mm^3 is rare. Normalization of the platelet count occurs within 12 weeks of delivery. Although the cause is uncertain, gestational thrombocytopenia may be due to accelerated platelet consumption. There is no risk of hemorrhage to the mother, fetus, or neonate. Antiplatelet antibodies often are detectable but this test does not differentiate gestational thrombocytopenia from immune thrombocytopenic purpura.

Preeclampsia accounts for approximately 20% of cases of pregnancy-associated thrombocytopenia. This condition is defined by new-onset hypertension with blood pressure greater than or equal to 140/90 mm Hg coupled with 1+ proteinuria on urine dip or a 24-hour collection containing 300 mg or more of protein. The hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome is a variant of preeclampsia. Neither condition is present in the patient described given her lack of hypertension, liver abnormality, or hemolysis.

Thrombocytopenia is present in approximately 25% of patients with systemic lupus erythematosus secondary to platelet destruction due to antiplatelet antibodies and circulating immune complexes. The described patient has Raynaud phenomenon but no other findings characteristic of systemic lupus erythematosus, which minimizes the likelihood of this diagnosis.

American College of Obstetricians and Gynecologists. Thrombocytopenia in pregnancy. ACOG Practice Bulletin 6. Washington, DC: ACOG; 1999.

Bockenstedt PL. Thrombocytopenia in pregnancy. Hematol Oncol Clin North Am 2011;25:293, 310, vii–viii.

Diagnosis and management of preeclampsia and eclampsia. ACOG Practice Bulletin No. 33. American College of Obstetricians and Gynecologists. Obstet Gynecol 2002;99:159–67.

Lockshin MD, Salmon JE, Erkan D. Pregnancy and rheumatic diseases. In: Creasy RK, Resnik R, Iams JD, eds. Creasy and Resnik's maternal–fetal medicine: principles and practice. 6th ed. Philadelphia (PA): Saunders Elsevier; 2009. p. 1081–3.

Reese JA, Li X, Hauben M, Aster RH, Bougie DW, Curtis BR, et al. Identifying drugs that cause acute thrombocytopenia: an analysis using 3 distinct methods. Blood 2010;116:2127–33.

39

Peripartum cardiomyopathy

A 38-year-old African American woman comes to your office for an incision check, 10 days after cesarean delivery for twins at term. The pregnancy was uncomplicated and her medical history is negative. She says she has fatigue, cough, generalized abdominal discomfort, and dyspnea that grows worse with exertion. On physical examination, blood pressure is 130/80 mm Hg and heart rate is 110 beats per minute; pedal edema is present. She is afebrile. The abdominal examination is nonfocal, and the incision is intact. You hear rales in both lung bases and note an occasional premature beat on auscultation of the heart. Chest X-ray shows cardiomegaly and increased pulmonary vascularity. Echocardiography shows a dilated left ventricle and an ejection fraction of 30%. The most important initial step in management is to administer

* (A) furosemide
(B) supplemental oxygen with bed rest
(C) levosimendan
(D) bromocriptine mesylate

The patient meets the criteria for peripartum cardiomyopathy, a disorder of uncertain etiology that affects one woman for every 3,000–4,000 live births in the United States. Criteria for diagnosis include the following:

- New-onset cardiac failure in the last month of pregnancy or the 5 months after giving birth
- Absence of another cause for heart failure
- Absence of preexisting cardiac disease
- Echocardiographic evidence of left ventricular systolic dysfunction (ie, ejection fraction less than 45%, impaired fractional shortening, and increased left ventricular end-diastolic dimension)

Although the cause is not established, certain factors are associated with an increased risk of peripartum cardiomyopathy, including African American or Caribbean ancestry, older maternal age, multiple pregnancy, the use of tocolytic drugs, and gestational hypertension or preeclampsia. A genetic predisposition has recently been suggested. Among the proposed etiologies of peripartum cardiomyopathy are viral myocarditis, immune-mediated myocardial injury, oxidative stress, and the production of a prolactin fragment, which is toxic to myocardium.

The major finding in peripartum cardiomyopathy is general heart failure. Other findings may include dyspnea, orthopnea, fatigue, dependent edema, nonproductive cough, tachypnea, tachycardia, palpitations, or chest pain. Blood pressure may be normal or increased; in later stages, hypotension is common. Oxygen desaturation may occur. Evidence of compromised peripheral circulation may manifest as abdominal pain because of bowel ischemia or infarction.

Most cases of peripartum cardiomyopathy present postpartum, and many are diagnosed late because symptoms may be confused with benign postpartum physiology. Diagnosis during pregnancy is challenging. In the course of evaluation, other causes of heart failure must be ruled out, such as hypertension, coronary artery disease, valvular disease, history of cardiotoxic chemotherapy or thoracic radiotherapy, lupus, and thyrotoxicosis. Signs of left-sided heart failure include rales and poor peripheral or end-organ perfusion; signs of right-sided heart failure include jugular venous distension, hepatosplenomegaly, and edema.

Chest X-ray is indicated to exclude other cardiac or pulmonary causes for symptoms, and to determine the degree of pulmonary vascular congestion. The current case definition, however, requires echocardiography. In low-resource settings where echocardiography is not easily available, peripartum cardiomyopathy may be overdiagnosed. Electrocardiography is performed because of the frequent association with arrhythmias and to rule out ischemic heart disease.

Laboratory tests include cardiac markers, such as creatinine kinase MB, cardiac troponins, and B-type natriuretic peptide. Arterial blood gas analysis may be indicated. In many cases, a noninvasive assessment of oxygen saturation is feasible (peripheral pulse oximetry) but in severe heart failure with peripheral vasoconstriction this may be impossible. Endomyocardial biopsy is not routinely performed, except in rare cases in which a specific entity (such as giant cell myocarditis) is to be ruled out.

Initial management is that of any heart failure. Large trials have not been conducted on treatment of peripartum

cardiomyopathy specifically. General goals are the following:

- Abolish or improve symptoms
- Achieve euvolemia
- Optimize hemodynamic state
- Ensure adequate oxygenation

Diuretics are first-line treatment in heart failure. If perfusion is otherwise adequate and blood pressure is within the normal range, a vasodilator, such as an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker is added. Although ACE inhibitors are known to improve survival in heart failure, neither ACE inhibitors nor angiotensin receptor blockers are given during pregnancy because of concerns for fetal safety. Hydralazine or nitrates may be used during pregnancy. Both of the ACE inhibitors captopril and enalapril are compatible with breastfeeding and may be used during the postpartum period; limited nonreassuring information is available about angiotensin receptor blocker in breastfeeding.

Beta-blockers, especially metoprolol, carvedilol, and bisoprolol, have been shown to decrease mortality in heart failure and, therefore, are recommended for all heart-failure patients unless specifically contraindicated. They may transiently worsen fluid overload and symptoms of heart failure and, therefore, should be started after euvolemia has been achieved. More experience has been reported during pregnancy and lactation with metoprolol than with other β-blockers. Generally, β-blockers are considered to be compatible with breastfeeding. Risks of β-blockers have been reported to include fetal bradycardia, hypoglycemia, and impaired growth. Optimization of the maternal medical condition trumps such concerns in most cases.

Patients who do not respond to oral agents may require intravenous vasodilators or inotropes. Levosimendan is an intravenous inodilator that has been useful in the treatment of other types of decompensated heart failure, after other therapies have failed. Although case series describe its use in peripartum cardiomyopathy, a small randomized trial did not find a difference in outcome.

Animal studies and a limited experience in humans have recently increased the possibility of using bromocriptine mesylate in peripartum cardiomyopathy. A proposed common pathway for the myocardial damage of peripartum cardiomyopathy involves unbalanced oxidative stress and activation of a protease called cathepsin D, which cleaves prolactin into fragments, including the proaptotic 16kDa form, thought to cause specific cardiac damage. Blocking prolactin with bromocriptine presents a novel approach to the treatment of peripartum cardiomyopathy. In a small controlled trial, women with postpartum peripartum cardiomyopathy randomized to standard heart failure therapy plus bromocriptine had better ejection fraction and better functional status than women who received standard heart failure therapy alone. Larger studies are currently under way. Bromocriptine also suppresses lactation. Women with peripartum cardiomyopathy are at heightened risk of thrombosis, and should receive thromboprophylaxis.

Biteker M, Duran NE, Kaya H, Gunduz S, Tanboga HI, Gokdeniz T, et al. Effect of levosimendan and predictors of recovery in patients with peripartum cardiomyopathy, a randomized clinical trial. Clin Res Cardiol 2011;100:571–7.

Carlin AJ, Alfirevic Z, Gyte GML. Interventions for treating peripartum cardiomyopathy to improve outcomes for women and babies. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD008589. DOI: 10.1002/14651858.CD008589.pub2.

Cruz MO, Briller J, Hibbard JU. Update on peripartum cardiomyopathy. Obstet Gynecol Clin North Am 2010;37:283–303. Goland S, Modi K, Bitar F, Janmohamed M, Mirocha JM, Czer LS, et al. Clinical profile and predictors of complications in peripartum cardiomyopathy. J Card Fail 2009;15:645–50.

Sliwa K, Blauwet L, Tibazarwa K, Libhaber E, Smedema JP, Becker A, et al. Evaluation of bromocriptine in the treatment of acute severe peripartum cardiomyopathy: a proof–of–concept pilot study [published erratum appears in Circulation 2010;121:e425]. Circulation 2010;121:1465–73.

Sliwa K, Hilfiker–Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. Heart Failure Association of the European Society of Cardiology Working Group on Peripartum Cardiomyopathy. Eur J Heart Fail 2010;12:767–78.

Yamac H, Bultmann I, Sliwa K, Hilfiker–Kleiner D. Prolactin: a new therapeutic target in peripartum cardiomyopathy. Heart 2010;96:1352–7.

40

Management of thrombophilia

You performed a repeat cesarean delivery on a 36-year-old woman, gravida 2, para 2, this morning. She has a history of venous thromboembolism in a prior pregnancy and is homozygous for the factor V Leiden mutation. She was maintained during the pregnancy on adjusted-dose low molecular weight heparin. She is planning on breastfeeding and asks whether she can avoid injectable anticoagulation. After her discharge, the best medication for her postpartum anticoagulation therapy is

* (A) warfarin sodium
(B) enoxaparin sodium
(C) heparin
(D) fondaparinux sodium
(E) aspirin

Factor V Leiden mutation is the most common genetic thrombophilia, with a prevalence of 5% in European populations and 3% in African Americans, although it is virtually absent in Asians and black Africans. It is also the most common cause for venous thromboembolism in pregnancy, accounting for nearly 40% of all cases.

Medical history and carrier status are the important determinants of the type of anticoagulation to be used, based on the risk of thromboembolism for each carrier state (Table 40-1). Further risk factors, such as a first-degree relative with a history of venous thromboembolism before age 50 years, obesity, prolonged immobility, or surgery, should also be taken into account when choosing an appropriate regimen.

In the postpartum period, unfractionated heparin, low molecular weight heparin, such as enoxaparin sodium, or warfarin sodium can each be used. None of the anticoagulants are excreted in breast milk, and all of the medications are compatible with breastfeeding. Heparin administration is typically initiated 4–6 hours after vaginal delivery or 6–12 hours after cesarean delivery, to limit concerns related to hemorrhage or hematoma formation.

TABLE 40-1. Venous Thromboembolism Risks and Management Principles for Pregnant Patients With Factor V Leiden Mutations

		No History of VTE	Prior VTE
Factor V Leiden heterozygote			
	VTE risk in pregnancy	Less than 0.3%	10%
	Antepartum management	Surveillance without anticoagulation, or prophylactic LMWH or UFH	Prophylactic or intermediate-dose LMWH/UFH or surveillance without anticoagulation
	Postpartum management	Surveillance without anticoagulation, or prophylactic LMWH or UFH if additional risk factors are present	Prophylactic LMWH/UFH or warfarin (INR 2.0–3.0)
Factor V Leiden homozygote			
	VTE risk in pregnancy	1.5%	17%
	Antepartum management	Prophylactic LMWH or UFH	Prophylactic, intermediate-dose, or adjusted dose LMWH/UFH
	Postpartum management	Prophylactic LMWH/UFH or warfarin (INR 2.0–3.0)	Continue antepartum dosing, or warfarin (INR 2.0–3.0)

Abbreviations: INR, international normalized ratio; LMWH, low molecular weight heparin; UFH, unfractionated heparin.

Modified from Inherited thrombophilias in pregnancy. Practice Bulletin No. 124. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:730–40.

Both low molecular weight heparin and unfractionated heparin are typically used for prophylaxis, although warfarin can be used for patients who have a strong desire to avoid injections.

This patient would require adjusted-dose heparin, but given the desire to avoid injections, warfarin would be appropriate. Although the use of warfarin in pregnancy is avoided because of teratogenic and fetal anticoagulation concerns, it can be used in the postpartum period. Warfarin does not appear to be excreted in breast milk and is safe for breastfeeding. Warfarin should be initiated after delivery and dose adjusted to achieve an international normalized ratio of 2.0–3.0. When initiating warfarin therapy, it is critical to maintain the dose of heparin at therapeutic levels for 5 days and until the international normalized ratio is therapeutic for 2 days, in order to avoid paradoxical thrombosis for the early antiprotein C effect of warfarin.

Fondaparinux sodium is a synthetic heparin typically reserved for patients with heparin allergies, with a history of heparin-induced thrombocytopenia, or who have failed other anticoagulants. Aspirin is not considered an appropriate anticoagulant for management of inherited thrombophilias.

Clark SL, Porter TF, West FG. Coumarin derivatives and breast–feeding. Obstet Gynecol 2000;95:938–40.

Dizon-Townson D, Miller C, Sibai B, Spong CY, Thom E, Wendel G Jr, et al. The relationship of the factor V Leiden mutation and pregnancy outcomes for mother and fetus. Obstet Gynecol 2005;106:517–24.

Gerhardt A, Scharf RE, Beckmann MW, Struve S, Bender HG, Pillny M, et al. Prothrombin and factor V mutations in women with a history of thrombosis during pregnancy and the puerperium. N Engl J Med 2000;342:374–80.

Inherited thrombophilias in pregnancy. Practice bulletin No. 124. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:730–40.

Zotz RB, Gerhardt A, Scharf RE. Inherited thrombophilia and gestational venous thromboembolism. Best Pract Res Clin Haematol 2003; 16:243–59.

41

Treatment of gestational diabetes mellitus

Gestational diabetes mellitus was diagnosed in a 32-year-old Latin American woman, gravida 1, at 28 weeks of gestation 2 weeks ago. She initiated a 2,000-kcal American Diabetes Association diet and has been monitoring her blood sugar with a home glucometer. Her fasting blood sugar ranges from 120 mg/dL to 140 mg/dL and her 2-hour postprandial sugar ranges from 170 mg/dL to 240 mg/dL. The best next step in management is

(A) increase the fiber content of her diet (35 g/day)
(B) begin a low carbohydrate diet (40 g/day)
(C) glyburide therapy
* (D) insulin therapy
(E) initiate daily exercise regimen

For pregnant women with an abnormal glucose tolerance test, a home glucometer provides a useful maternal metabolic surveillance tool to detect hyperglycemia. Daily self-monitoring with a home glucometer is preferable to intermittent office monitoring.

Consultation with a nutritionist with individualization of medical nutrition therapy constitutes first-line intervention. Intake of 35 kcal/kg (approximately 2,000–2,500 kcal per day) in a diet that consists of 50–60% carbohydrates usually will be adequate. Normal weight women should eat adequate calories to avoid ketone production, but it has been suggested that obese patients may undergo a calorically restrictive diet. Avoiding excessive ketonuria or weight loss, even in the obese patient, may be prudent. Artificial sweeteners may be used in a limited fashion. Dietary fiber is believed to slow carbohydrate absorption and blunt glucose extremes and can be useful for patients with type 2 diabetes mellitus. However, research has not proved that increase in dietary fiber intake and reduction of carbohydrate intake would benefit women with gestational diabetes.

Exercise generally is considered to be beneficial for patients with type 2 diabetes and may offer benefits for pregnant women. Exercise in patients with gestational

diabetes can lower blood sugar. It is not considered a substitute for medical therapy for hyperglycemia in pregnancy.

When nutrition therapy fails, medical therapy is initiated with either insulin or select oral hypoglycemic agents. Health care providers disagree on the level of hyperglycemia at which to add medical therapy, but generally fasting hyperglycemia greater than 105 mg/dL or 2-hour levels that exceed 120–130 mg/dL are suggested as thresholds for initiation of medication. For more elevated glucose levels, insulin is generally recommended and the dose is adjusted based on self-glucose monitoring levels.

Oral hypoglycemic agents, such as glyburide, are more simply administered than injectable insulin and, thus, provide better patient adherence. However, oral hypoglycemic agents have been shown to have high failure rates (in the 20% range) in achieving euglycemia in women with elevated fasting glucose. For this patient, given her fasting glycemia, insulin therapy is the best choice. In women with gestational diabetes mellitus without elevated fasting glucose or obesity, glyburide compares favorably with insulin with respect to pregnancy outcomes. Metformin, a biguanide, is an insulin sensitizer, not a secretagogue, and has been reported to provide effective glycemic control in gestational diabetes. Although glyburide and metformin cross the placenta, the rates of neonatal hypoglycemia are not higher than in mothers treated with insulin. The National Institutes of Health is considering potential changes in screening for glucose intolerance in pregnancy.

Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. N Engl J Med 2005;352:2477–86.

Dhulkotia JS, Ola B, Fraser R, Farrell T. Oral hypoglycemic agents vs insulin in management of gestational diabetes: a systematic review and metaanalysis. Am J Obstet Gynecol 2010;203:457.e1–9.

Gestational diabetes. ACOG Practice Bulletin No. 30. American College of Obstetricians and Gynecologists. Obstet Gynecol 2001;98:525–38.

Gestational diabetes mellitus. American Diabetes Association. Diabetes Care 2004;27 Suppl 1:S88–90.

Gestational diabetes mellitus. American Diabetes Association. Diabetes Care 2003;26 Suppl 1:S103–5.

Metzger BE, Buchanan TA, Coustan DR, de Leiva A, Dunger DB, Hadden DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus [published erratum appears in Diabetes Care 2007;30:3154]. Diabetes Care 2007;30(suppl 2):S251–60.

Nicholson W, Baptiste-Roberts K. Oral hypoglycaemic agents during pregnancy: The evidence for effectiveness and safety. Best Pract Res Clin Obstet Gynaecol 2011;25:51–63.

Rowan JA, Hague WM, Gao W, Battin MR, Moore MP. Metformin versus insulin for the treatment of gestational diabetes. MiG Trial Investigators [published erratum appears in N Engl J Med 2008;359:106]. N Engl J Med 2008;358:2003–15.

Wensel TM. Role of metformin in the treatment of gestational diabetes. Ann Pharmacother 2009;43:939–43.

42

Genital herpes in patient with preterm premature rupture of membranes

A 32-year-old pregnant woman at 26 weeks of gestation comes to the labor and delivery unit with leakage of fluid. The fetal monitor shows a reassuring fetal heart rate tracing and no contractions. Sterile speculum examination reveals moderate clear fluid (nitrazine positive, ferning on microscopy) in the vagina with a closed cervix. On removal of the speculum, a cluster of 3 shallow ulcers are noted on the right labium. The patient reports that this is her usual location of herpes outbreaks and that she has experienced burning in that area for 24 hours. The best next step in management is

(A) culture the lesions and await results
(B) administer betamethasone and perform cesarean delivery in 48 hours
(C) immediate cesarean delivery
* (D) immediate antiviral therapy
(E) antiviral therapy at 34 weeks of gestation

Herpes simplex transmission to the newborn can occur during the antenatal, intrapartum, or neonatal periods. Close to 85% of neonatal herpes infections occur during labor. Neonates can develop local disease of the skin, eye, or mouth; they also can develop devastating encephalitis or disseminated herpes. Fortunately, neonatal herpes is uncommon, ranging from 1 in 3,200 to 1 in 20,000 live births. Approximately two thirds of cases of neonatal herpes are due to herpes simplex virus type 2 (HSV-2) with the remainder due to herpes simplex virus type 1 (HSV-1). Approximately 17–25% of all pregnant women in the United States have serologic evidence of HSV-2, and approximately 2% of susceptible women will develop laboratory confirmed evidence of HSV-2 infection during their new pregnancy. Primary infections late in pregnancy confer the greatest risk of infection to the neonate, but even asymptomatic viral shedding has the potential to lead to neonatal infection. The presence of type-specific maternal antibody found with recurrent herpes likely decreases but does not eliminate the risk to the neonate. Risk of transmission to the neonate with a vaginal delivery in the setting of asymptomatic viral shedding is 2 in 10,000, but with active lesions from recurrent disease the risk is 0–3%. Cesarean delivery performed for active lesions before labor or rupture of membranes is effective at preventing neonatal disease.

At term with rupture of membranes and active herpes, recommendations are to perform a cesarean delivery preferably within 4–6 hours of premature rupture of membranes (PROM) to reduce the risk of neonatal herpes, although cesarean delivery may be beneficial regardless of the duration of rupture of membranes. In the event of preterm PROM in a woman with genital herpes, the risk of prematurity may exceed the risk of neonatal herpes. In a case series of 29 pregnant women with preterm PROM with a mean gestational age of 27 weeks and development of recurrent HSV-2, no neonates had evidence of herpes infection despite expectant management and inconsistent use of acyclovir (8 out of 29 mothers were on varying acyclovir regimens). In that study, 40% of neonates had major morbidity related to prematurity that likely would have been worse if immediate delivery had been pursued. Therefore, cesarean delivery either immediately or after administration of steroids is not the best next step.

The aforementioned data were collected in women with recurrent herpes. Expectant management of preterm PROM in the setting of primary infection with heavy viral shedding and no maternal antibody would be predicted to be risky for development of neonatal herpes. The duration of antiviral treatment and optimal timing of delivery for a woman with recurrent herpes and preterm PROM has not been determined.

In an individual with first-occurrence genital ulcer disease, herpes identification by culture or polymerase chain reaction of the lesion may be useful to confirm the diagnosis. Herpes culture in recurrent disease has a 40% sensitivity. There is no need to wait for results in order to start antiviral therapy.

Acyclovir, valacyclovir, and famciclovir are effective at decreasing the risk of active lesions (reduced by 75%) and viral shedding (reduced by 90%) in late pregnancy and may be used in the setting of preterm PROM. Antiviral therapy should be started immediately and should not wait until 34 weeks of gestation. Table 42-1 lists recommended treatment dosages. Corticosteroids for fetal lung maturation also have been used in the setting of recurrent herpes and ruptured membranes without resulting neonatal herpes.

TABLE 42-1. Recommended Regimens for Antiviral Therapy for First Clinical Episode, Recurrent Episode, and Suppression of Genital Herpes

Drug	First Episode	Recurrent Episode	Suppression
Acyclovir	Oral, 400 mg three times a day for 7–10 days	Oral, 400 mg three times a day for 5 days	Oral, 400 mg twice a day
Famciclovir	Oral, 250 mg three times a day for 7–10 days	Oral, 1,000 mg twice a day for two doses	Oral, 250 mg twice a day
Valacyclovir	Oral, 1,000 mg twice a day for 10 days	Oral, 500 mg twice a day for 3 days	Oral, 500–1,000 mg daily

Modified from Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. Centers for Disease Control and Prevention [published erratum appears in MMWR Morb Mortal Wkly Rep 2011;60:18]. MMWR Recomm Rep 2010;59:1–110.

Anzivino E, Fioriti D, Mischitelli M, Bellizzi A, Barucca V, Chiarini F, et al. Herpes simplex virus infection in pregnancy and in neonate: status of art of epidemiology, diagnosis, therapy and prevention. Virol J 2009;6:40.

Major CA, Towers CV, Lewis DF, Garite TJ. Expectant management of preterm premature rupture of membranes complicated by active recurrent genital herpes. Am J Obstet Gynecol 2003;188:1551–4; discussion 1554–5.

Management of herpes in pregnancy. ACOG Practice Bulletin No. 82. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;109:1489–98.

Premature rupture of membranes. ACOG Practice Bulletin No. 80. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;109:1007–19.

Sheffield JS, Hill JB, Hollier LM, Laibl VR, Roberts SW, Sanchez PJ, et al. Valacyclovir prophylaxis to prevent recurrent herpes at delivery: a randomized clinical trial [published erratum appears in Obstet Gynecol 2006;108:695]. Obstet Gynecol 2006;108:141–7.

Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. Centers for Disease Control and Prevention [published erratum appears in MMWR Morb Mortal Wkly Rep 2011;60:18]. MMWR Recomm Rep 2010;59:1–110.

43

Toxoplasmosis and pregnancy

A 26-year-old primigravid woman at 19 weeks of gestation comes to your office for a follow-up prenatal visit. She has three outdoor cats and is responsible for changing the cat litter. A week ago her family practice physician ordered toxoplasma serology. She tested positive for immunoglobulin M (IgM) antibodies but negative for immunoglobulin G (IgG) antibodies. She has read about the risks of toxoplasmosis in pregnancy and is concerned about transmission to the fetus. She has no systemic symptoms. The next step in her management related to this concern is

(A) detailed fetal anatomic ultrasonography
(B) toxoplasma antigen polymerase chain reaction testing of amniotic fluid
* (C) maternal toxoplasma-specific IgG and IgM antibody testing at reference laboratory
(D) spiramycin treatment
(E) pyrimethamine–sulfadiazine treatment

Toxoplasma gondii is an intracellular parasite that complicates 0.1–1.0% of pregnancies in the United States. Acute *T gondii* infection in immunocompetent patients often involves influenza-like symptoms or is subclinical. In immunosuppressed patients, infection may present as encephalitis, myocarditis, pneumonitis, or hepatitis. Congenital toxoplasmosis may manifest as chorioretinitis, blindness, deafness, seizures, convulsions, hydrocephalus, microcephaly, fever, jaundice, hepatosplenomegaly, pneumonitis, or coagulopathy. Most cases are asymptomatic, but 15% of cases are considered severe. In pregnancy, there is an increased risk of miscarriage, stillbirth, intrauterine growth restriction, and preterm birth.

Oocysts are found only in cats; trophozoites are the invasive protozoan forms and can infect feline or human muscle and brain tissue, where they form cysts. Transmission to humans occurs by ingestion of infected raw or undercooked meat (eg, lamb, pork, beef), or exposure to cat feces in cat litter or contaminated soil. Prevention can reduce the transmission rate by as much as 60%; this includes wearing gloves during gardening and washing hands afterwards, avoiding contact with cat litter, thoroughly cooking meats, and washing fruits and vegetables.

Congenital infection may occur if a woman develops acute toxoplasmosis in pregnancy, or in chronic toxoplasmosis in an immunocompromised host. Transplacental transmission only occurs in primary infections (except in the immunocompromised) and there is a 40% risk if the infection is acquired in pregnancy (transmission rate of 15–20% if acquired in the first trimester and 65% if acquired in the third trimester). Conversely, although the risk of transmission increases later in gestation, the severity of the congenital infection increases with decreasing gestational age.

Routine screening for toxoplasmosis in pregnancy is not recommended, except in patients with human immunodeficiency virus (HIV). Routine screening is complicated by a high baseline rate of prior infection (40%), persistence of IgM antibodies long after an acute infection, and an IgM false-positive rate of up to 88% in some commercially available tests. Patients that are symptomatic or at particularly high risk can be tested, given that this increased pretest probability will improve the performance of the test.

Testing this patient for toxoplasma-specific antibodies 2 weeks after the prior studies will aid in counseling and management. Confirmatory testing of toxoplasma-specific antibody using a reference standard (as offered by the Palo Alto Medical Foundation; www.pamf.org/serology) improves the specificity of the test.

Positive IgM and IgG test results would indicate a recent infection. Negative IgM and IgG test results would indicate that the first IgM test result was false-positive. Similarly, a positive persistent, isolated IgM test result would also indicate that the initial IgM test result was false-positive. Targeted anatomic ultrasonography may be performed in order to screen for ultrasonographic indicators of congenital infection (eg, IUGR, microcephaly, intracranial calcifications, hydrocephalus), but would not be the next step in management. Amniotic fluid testing or antimicrobial treatment (eg, with spiramycin or pyrimethamine–sulfadiazine) should not be considered without confirmed serologic or ultrasonographic findings.

American College of Obstetricians and Gynecologists. Perinatal viral and parasitic infections. ACOG Practice Bulletin 20. Washington, DC: ACOG; 2000.

Garry DJ, Elimian A, Wiencek V, Baker DA. Commercial laboratory IgM testing for Toxoplasma gondii in pregnancy: a 20–year experience. Infect Dis Obstet Gynecol 2005;13:151–3.

Montoya JG, Liesenfeld O. Toxoplasmosis. Lancet 2004;363:1965–76.

44

Group B streptococci and penicillin allergy

A 34-year-old primigravid woman at 38 weeks of gestation comes to the hospital in active labor. She moved to the area recently and has not yet established prenatal care in your office. Her previous obstetrician called to inform her that her genital culture at 36 weeks of gestation was positive for group B streptococci (GBS). She has a penicillin allergy, which she describes as an itchy raised rash (hives). You obtain a copy of her culture report, which shows that the GBS isolate is sensitive to both erythromycin and clindamycin. The best antibiotic to use for GBS prophylaxis during her labor is

(A) cefazolin
* (B) clindamycin
(C) erythromycin
(D) penicillin G
(E) vancomycin

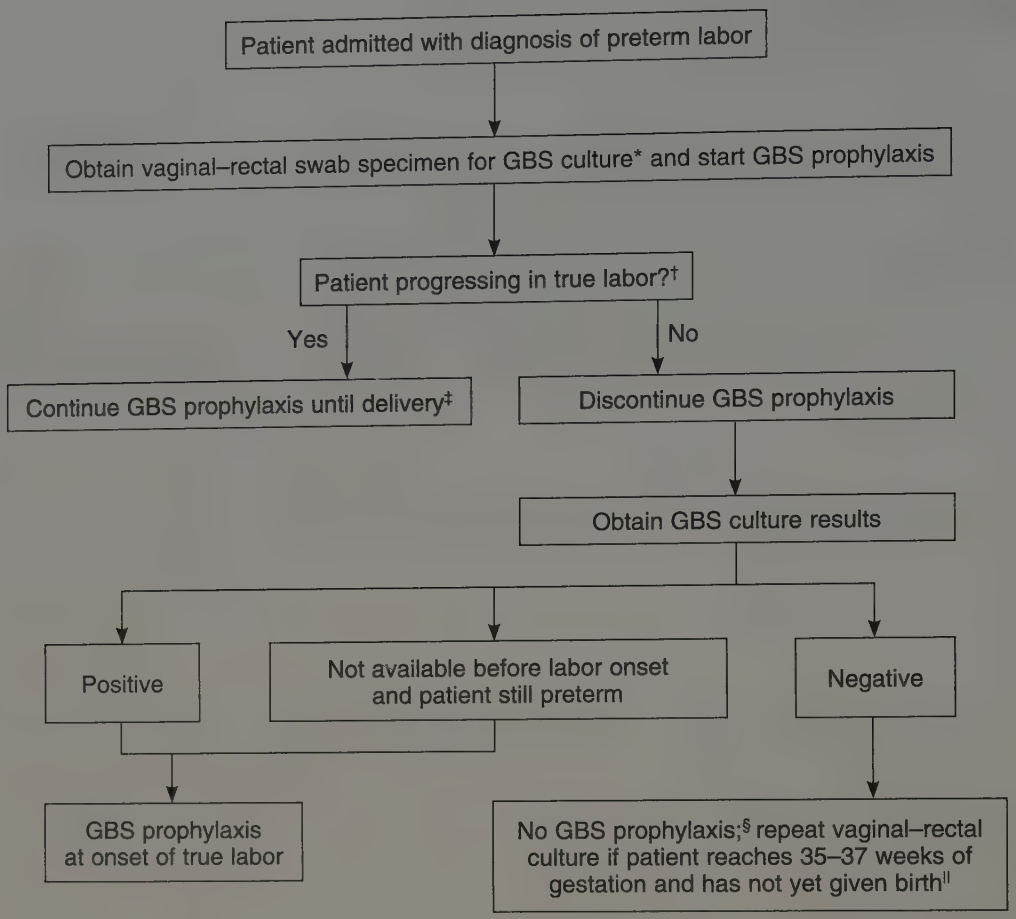
Group B streptococcal sepsis is the leading cause of early-onset neonatal sepsis in the United States. The causative agent, *Streptococcus agalactiae*, often is found in the gastrointestinal tract and colonizes the vagina in some individuals. Colonization may be intermittent or chronic and occurs in 10–30% of pregnant patients. Colonized patients usually are asymptomatic but may experience urinary tract infection, amnionitis, endometritis, sepsis, or meningitis. Neonates whose mothers have group B streptococcal colonization are at risk of early-onset group B streptococcal disease, including sepsis, pneumonia, and meningitis. Substantial reductions in disease burden have occurred since the 1990s, when the first set of prevention guidelines from the Centers for Disease Control and Prevention was published. Current incidence estimates of early-onset group B streptococcal disease are similar to estimates of late-onset group B streptococcal disease, around 0.5 cases per 1,000 live births. Revisions in 2002 included recommendations for a universal screening policy to culture all pregnant women between 35 weeks and 37 weeks of gestation for the presence of GBS. The exceptions to universal screening are patients who have had either group B streptococcal bacteruria during the current pregnancy or an infant affected by invasive group B streptococcal disease.

The Centers for Disease Control and Prevention released its third set of guidelines for GBS sepsis prevention in 2010. The newest guidelines included updated information on laboratory testing, an inoculum threshold for urine culture reporting of GBS in pregnancy, updated algorithms for preterm labor (Fig. 44-1) and preterm premature rupture of membranes (Fig. 44-2), dosing changes for penicillin-G, new recommendations for treating GBS-positive patients with a penicillin allergy (Fig. 44-3), and updated management guidelines for newborns. Laboratory guidance now includes the use of nucleic acid amplification testing for identification of GBS colonization. Reporting guidelines for GBS bacteruria recommended reporting the presence of any colonies, but this strategy was unique to GBS for laboratories that otherwise used a threshold of 10^4 colony-forming units/mL for other pathogens. The extra laboratory workload and lack of supportive data for screening for low colony-count GBS colonization led to the revision that now includes a threshold of 10^4 colony-forming units/mL for group B streptococcal bacteruria reporting. Patients should receive antibiotic prophylaxis in labor if they have a positive GBS test result. Other recommendations for prophylaxis are provided in Table 44-1.

For the described patient, her penicillin allergy eliminates the possibility of administering penicillin. The guidelines recommend avoiding cefazolin in high-risk penicillin allergies, such as this patient's urticarial reaction. If isolates are tested for susceptibility to clindamycin and erythromycin and found to be sensitive, erythromycin is no longer recommended. Clindamycin, therefore, should be used. Vancomycin should be reserved for cases in which the sensitivity testing to clindamycin and erythromycin are not known. If a GBS isolate is susceptible to clindamycin and resistant to erythromycin, and D-zone testing for inducible resistance has been performed with a negative test result (no inducible resistance), clindamycin can be used for GBS intrapartum prophylaxis instead of vancomycin.

Prevention of early-onset group B streptococcal disease in newborns. Committee Opinion No. 485. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:1019–27.

Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010, Centers for Disease Control and Prevention. MMWR Recomm Rep 2010;59:1–36.


Patient admitted with diagnosis of preterm labor
Obtain vaginal–rectal swab specimen for GBS culture* and start GBS prophylaxis
Patient progressing in true labor?†
Yes
No
Continue GBS prophylaxis until delivery‡
Discontinue GBS prophylaxis
Obtain GBS culture results
Positive
Not available before labor onset and patient still preterm
Negative
GBS prophylaxis at onset of true labor
No GBS prophylaxis;§ repeat vaginal–rectal culture if patient reaches 35–37 weeks of gestation and has not yet given birth‖

*If patient has undergone vaginal–rectal GBS culture within the preceding 5 weeks, the results of that culture should guide management. GBS-colonized women should receive intrapartum antibiotic prophylaxis. No antibiotics are indicated for GBS prophylaxis if the result of a vaginal–rectal screen within 5 weeks was negative.

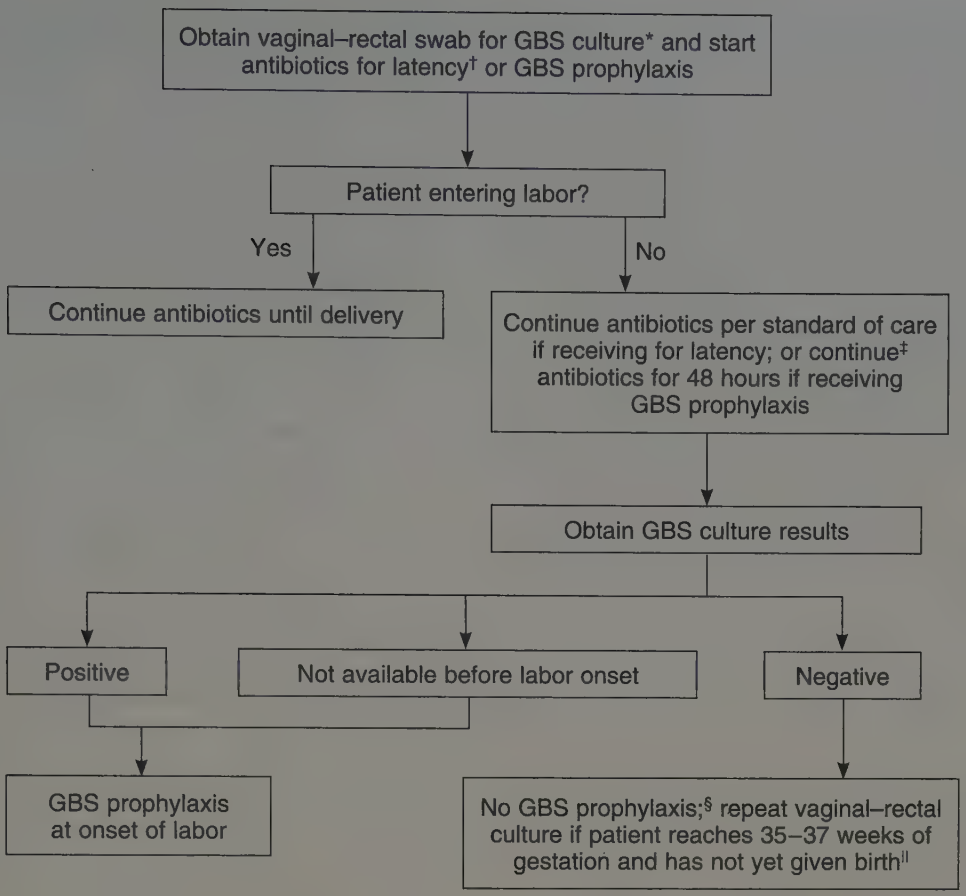
†Patient should be regularly assessed for progression to true labor; if the patient is considered not to be in true labor, discontinue GBS prophylaxis.

‡If GBS culture results become available before delivery and are negative, then discontinue GBS prophylaxis.

§Unless subsequent GBS culture result before delivery is positive

‖A negative GBS screen result is considered valid for 5 weeks. If a patient with a history of preterm labor is readmitted with signs and symptoms of preterm labor and had a negative GBS screen result more than 5 weeks prior, she should be rescreened and managed according to this algorithm at that time.

Fig. 44-1. Algorithm for group B streptococci intrapartum prophylaxis for women in preterm labor. Abbreviation: GBS, group B streptococci. (Data from Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep 2010;59(RR–10):1–36.)


Obtain vaginal–rectal swab for GBS culture* and start antibiotics for latency† or GBS prophylaxis
Patient entering labor?
Yes
No
Continue antibiotics until delivery
Continue antibiotics per standard of care if receiving for latency; or continue‡ antibiotics for 48 hours if receiving GBS prophylaxis
Obtain GBS culture results
Positive
Not available before labor onset
Negative
GBS prophylaxis at onset of labor
No GBS prophylaxis;§ repeat vaginal–rectal culture if patient reaches 35–37 weeks of gestation and has not yet given birth‖

*If patient has undergone vaginal–rectal GBS culture within the preceding 5 weeks, the results of that culture should guide management. GBS-colonized women should receive intrapartum antibiotic prophylaxis. No antibiotics are indicated for GBS prophylaxis if the result of a vaginal–rectal screen within 5 weeks was negative.

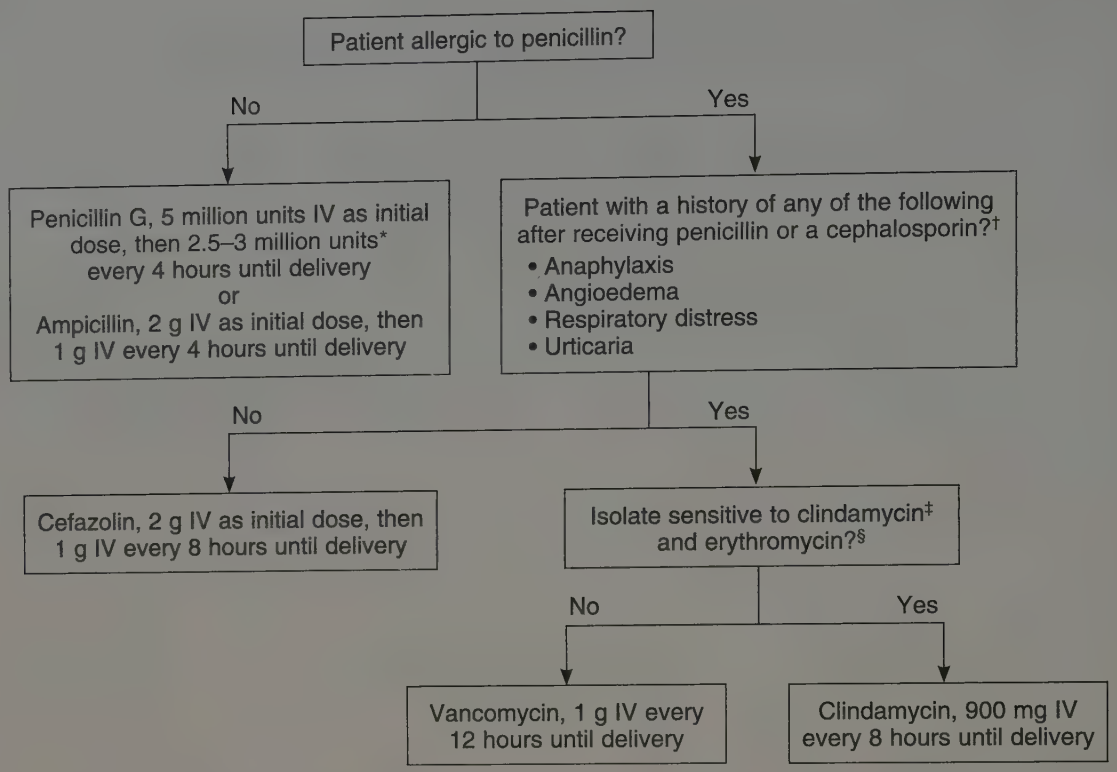
†Antibiotics given for latency in the setting of preterm premature rupture of membranes that include ampicillin, 2 g intravenously once, followed by 1 g intravenously every 6 hours for at least 48 hours are adequate for GBS prophylaxis. If other regimens are used, GBS prophylaxis should be initiated in addition.

‡GBS prophylaxis should be discontinued at 48 hours for women with preterm premature rupture of membranes who are not in labor. If results from a GBS screen performed on admission become available during the 48-hour period and are negative, GBS prophylaxis should be discontinued at that time.

§Unless subsequent GBS culture result before delivery is positive

‖A negative GBS screen result is considered valid for 5 weeks. If a patient with preterm premature rupture of membranes is entering labor and had a negative GBS screen result more than 5 weeks prior, she should be rescreened and managed according to this algorithm at that time.

Fig. 44-2. Algorithm for group B streptococci intrapartum prophylaxis for women with preterm premature rupture of membranes. Abbreviation: GBS, group B streptococci. (Data from Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep 2010;59(RR–10):1–36.)


Patient allergic to penicillin?
No
Yes
Penicillin G, 5 million units IV as initial dose, then 2.5–3 million units* every 4 hours until delivery
or
Ampicillin, 2 g IV as initial dose, then 1 g IV every 4 hours until delivery
Patient with a history of any of the following after receiving penicillin or a cephalosporin?†
• Anaphylaxis
• Angioedema
• Respiratory distress
• Urticaria
No
Yes
Cefazolin, 2 g IV as initial dose, then 1 g IV every 8 hours until delivery
Isolate sensitive to clindamycin‡ and erythromycin?§
No
Yes
Vancomycin, 1 g IV every 12 hours until delivery
Clindamycin, 900 mg IV every 8 hours until delivery

*Doses ranging from 2.5 million units to 3.0 million units are acceptable for the doses administered every 4 hours following the initial dose. The choice of dose within that range should be guided by which formulations of penicillin G are readily available in order to reduce the need for pharmacies to specially prepare doses.

†Penicillin-allergic patients with a history of anaphylaxis, angioedema, respiratory distress, or urticaria following administration of penicillin or a cephalosporin are considered to be at high risk of anaphylaxis and should not receive penicillin, ampicillin, or cefazolin for group B streptococci (GBS) intrapartum prophylaxis. For penicillin-allergic patients who do not have a history of those reactions, cefazolin is the preferred agent because pharmacologic data suggest it achieves effective intraamniotic concentrations. Vancomycin and clindamycin should be reserved for penicillin-allergic women at high risk of anaphylaxis.

‡If laboratory facilities are adequate, clindamycin and erythromycin susceptibility testing should be performed on prenatal GBS isolates from penicillin-allergic women at high risk of anaphylaxis. If no susceptibility testing is performed, or the results are not available at the time of labor, vancomycin is the preferred agent for GBS intrapartum prophylaxis for penicillin-allergic women at high risk of anaphylaxis.

§Resistance to erythromycin is often but not always associated with clindamycin resistance. If an isolate is resistant to erythromycin, it may have inducible resistance to clindamycin, even if it appears susceptible to clindamycin. If a GBS isolate is susceptible to clindamycin, resistant to erythromycin, and D-zone testing for inducible resistance has been performed and the result is negative (no inducible resistance), then clindamycin can be used for GBS intrapartum prophylaxis instead of vancomycin.

Fig. 44-1. Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal disease (broader spectrum agents, including an agent active against group B streptococci, may be necessary for treatment of chorioamnionitis). Abbreviation: IV, intravenous. (Data from Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep 2010;59(RR–10):1–36.)

TABLE 44-1. Indications and Nonindications for Intrapartum Antibiotic Prophylaxis to Prevent Early-Onset Group B Streptococcal Disease

Intrapartum GBS Prophylaxis Indicated	Intrapartum GBS Prophylaxis not Indicated
Previous infant with invasive GBS disease	Colonization with GBS during a previous pregnancy (unless an indication for GBS prophylaxis is present for current pregnancy)
GBS bacteriuria during any trimester of the current pregnancy	GBS bacteriuria during previous pregnancy (unless another indication for GBS prophylaxis is present for current pregnancy)
Positive GBS screening culture during current pregnancy* (unless a cesarean delivery, is performed before onset of labor on a woman with intact amniotic membranes)	Cesarean delivery performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age
Unknown GBS status at the onset of labor (culture not done, incomplete, or results unknown) and any of the following: • Delivery at less than 37 weeks of gestation • Amniotic membrane rupture greater than or equal to 18 hours • Intrapartum temperature greater than or equal to 100.4°F (greater than or equal to 38.0°C)† • Intrapartum NAAT‡ positive for GBS	Negative vaginal and rectal GBS screening culture result in late gestation* during the current pregnancy, regardless of intrapartum risk factors

Abbreviations: GBS, group B streptococci; NAAT, nucleic acid amplification test.

* Optimal timing for prenatal GBS screening is at 35–37 weeks of gestation.

† If amnionitis is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis.

‡ NAAT testing for GBS is optional and may not be available in all settings. If intrapartum NAAT result is negative for GBS but any other intrapartum risk factor (delivery at less than 37 weeks of gestation, amniotic membrane rupture at 18 hours or more, or temperature greater than or equal to 100.4°F [greater than or equal to 38.0°C]) is present, then intrapartum antibiotic prophylaxis is indicated.

Data from Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep 2010;59(RR–10):1–36.

45

Human immunodeficiency virus

A 30-year-old nulligravid woman presents to your office for preconception counseling. After 2 years together, she and her partner are ready to begin a family. She is human immunodeficiency virus (HIV)-negative and her partner is HIV-positive. The couple has been using condoms for contraception. She has no medical, surgical, or gynecologic history that would affect obstetric management. The best next step in management of this patient is to

(A) prescribe zidovudine
(B) counsel against pregnancy
(C) advise the couple to discontinue condom use
* (D) refer for assisted reproductive technology (ART)
(E) recommend circumcision for the male partner

Human immunodeficiency virus is a serious and lifelong disease which is both sexually and vertically transmissible. Most individuals with HIV are in their reproductive years, and many express a desire to become parents. The decision to have children is an intensely felt personal goal for many women, and the physician cannot substitute his/her own decisions and values without overstepping the ethical bounds of patient autonomy. Furthermore, a refusal to discuss options of interest to the patient risks driving her decision-making underground: she is then unlikely to present for appropriate medical care when it is indicated. Thus, one cannot simply counsel against pregnancy. In some circumstances, the physician might recommend donor insemination, but in the described scenario, the patient and her partner want to have a child together.

A woman's risk of acquiring HIV infection from an HIV-positive male partner is estimated to be less than 1 in 500 unprotected coital acts. That risk is subject to modification by factors such as concomitant genital infection or abrasion, and the viral load of the affected partner. A plan to stop using condoms and attempt natural conception imposes the risk of infection upon the uninfected partner. Even a strategy that restricts unprotected intercourse to the time of ovulation has been associated with a 4% risk that the woman will seroconvert and, therefore, is unsafe.

In high-prevalence areas, male circumcision has been demonstrated to reduce the risk of HIV acquisition by the male partner, but male circumcision is not known to reduce the risk that an infected male will transmit HIV to an uninfected female. The role of male circumcision in low-prevalence high-resource areas such as the United States is unknown.

A number of ART methods have been described for achieving pregnancy in serodiscordant couples. These include sperm testing by polymerase chain reaction followed by intrauterine insemination of the seronegative female partner and in vitro fertilization with intracytoplasmic sperm injection after sperm washing. Small series show these methods have been as much as 100% effective in preventing HIV transmission from an HIV-positive male to an HIV-negative female. As would be expected with HIV-negative mothers, no HIV-positive infants have been born after conception with ART.

Assisted reproductive technology is expensive and may not be covered by insurance. In lower-resource settings, a strategy of harm reduction has been proposed, in order to make unprotected intercourse less risky for the uninfected female partner. This may include evaluation and treatment of coexisting ulcerative genital infections, limiting intercourse to the predicted time of ovulation, and getting the infected male partner on antiretroviral medications. Although neither the American College of Obstetricians and Gynecologists nor the Centers for Disease Control and Prevention recommends this approach, some experts state that natural conception could now be considered a viable alternative for HIV-serodiscordant couples, in the event that complete suppression of viremia is achieved in the HIV-positive partner. Efficiency of HIV transmission (either horizontally or vertically) is greatly affected by reduction in viral replication; in a Ugandan study, transmission to female partners varied 10-fold depending on the male partner's viral load.

The American Society of Reproductive Medicine recently updated guidelines for providing infertility care to couples in which one or both partners is HIV-positive. The guidelines follow years of improvement in the chronic management of HIV infection and in reducing mother-to-child transmission. The new guidelines endorse the desire of HIV-positive individuals to have their own genetically related children, and suggest they seek infertility care at "institutions with the facilities that

can provide the most effective evaluation, treatment, and follow-up."

Recently, there has been interest in the use of pre-exposure prophylaxis to prevent HIV transmission. In a randomized placebo-controlled trial of men who have sex with men, a fixed-drug combination of tenofovir disoproxil fumarate and emtricitabine has been shown to decrease the probability of acquiring HIV infection by 44%. In a multicenter randomized controlled trial of heterosexual HIV-discordant couples, implementation of a regimen of combination antiretroviral drugs for the patient with HIV was seen to reduce the risk of transmission to the sexual partner by 90%. Zidovudine has not been proposed for pre-exposure prophylaxis; its major use is in labor with HIV-positive women because it has been shown to decrease the risk of mother-to-child transmission.

Barreiro P, Castilla JA, Labarga P, Soriano V. Is natural conception a valid option for HIV-serodiscordant couples? Hum Reprod 2007; 22:2353–8.

Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. HPTN 052 Study Team. N Engl J Med 2011;365: 493–505.

Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. iPrEx Study Team. N Engl J Med 2010;363:2587–99.

Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet 2007;369:657–66.

Gray RH, Wawer MJ, Brookmeyer R, Sewankambo NK, Serwadda D, Wabwire–Mangen F, et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. Rakai Project Team. Lancet 2001;357:1149–53.

Human immunodeficiency virus and infertility treatment. Ethics Committee of the American Society for Reproductive Medicine. Fertil Steril 2010;94:11–5.

Matthews LT, Baeten JM, Celum C, Bangsberg DR. Periconception pre-exposure prophylaxis to prevent HIV transmission: benefits, risks, and challenges to implementation. AIDS 2010;24:1975–82.

Matthews LT, Mukherjee JS. Strategies for harm reduction among HIV-affected couples who want to conceive. AIDS Behav 2009;13 Suppl 1:5–11.

46

Management of triplets

You are counseling a patient at 16 weeks of gestation who has been recently informed that she is pregnant with triplets after insemination using assisted reproductive technology (ART). The couple suffered from azoospermia. She smokes 10 cigarettes per day and works as a teacher's assistant at a preschool. She had a prepregnancy weight of 56.7 kg (125 lb). You advise her that the most effective lifestyle modification she could undertake to prevent the preterm birth of her triplets would be

(A) no sexual activity
(B) bed rest for 4 hours per day beginning at 20 weeks of gestation
* (C) stop smoking
(D) gain more than 27 kg (60 lb)

Higher order multifetal gestations have up to a 50% risk of preterm birth. Although many authorities recommend limitations in activity or larger than normal maternal weight gains, none of these therapies have been proven to be effective in randomized control trials. Many lifestyle modifications have the potential for biologic harm and certainly can harm the patient's employment or relationships. Smoking is an additive risk factor for preterm birth and trials of smoking cessation have shown that successful quitters can lower their likelihood of having a low birth weight baby, thus smoking cessation would be the lifestyle intervention of choice for the described patient. She should be referred for smoking cessation counseling and, failing that, should be offered pharmacotherapy. First-line pharmacotherapy to enhance smoking cessation in pregnancy would include either nicotine replacement or bupropion.

Both physical and sexual activity have been theorized to be causes or accelerants of preterm birth. However, controlled epidemiologic studies have shown that neither form of activity is a risk factor for preterm birth.

Bed rest is used by obstetricians and patients to treat a variety of perinatal conditions despite a lack of evidence of its efficacy. Other than forestalling the development of severe preeclampsia in patients with mild disease, no data support the effectiveness of bed rest. Complications caused by bed rest include loss of muscle mass, psychosocial isolation, employment difficulties, and possible

venous thromboembolic disease. Often, patients choose to treat themselves with bed rest based on cultural and familial beliefs. Health care providers should warn their patients about this common but ill-informed advice.

Recommendations for large weight gains are common from experts who explore the relationships between weight gain and perinatal outcome. Although there seems to be an association indicating that the more weight a nonobese pregnant woman gains the better, causality has not been proven. Given that a growing fetus contributes significantly to maternal weight and that fetal weight increases with gestational age, such a relationship could be spurious and not causal.

Chomitz VR, Cheung LW, Lieberman E. The role of lifestyle in preventing low birth weight. Future Child 1995;5:121–38.

Coleman T, Chamberlain C, Cooper S, Leonardi-Bee J. Efficacy and safety of nicotine replacement therapy for smoking cessation in pregnancy: systematic review and meta-analysis. Addiction 2011;106: 52–61.

Goodnight W, Newman R, Society of Maternal–Fetal Medicine. Optimal nutrition for improved twin pregnancy outcome. Obstet Gynecol 2009;114:1121–34.

Multiple gestation: complicated twin, triplet, and high-order multifetal pregnancy. ACOG Practice Bulletin No. 56. American College of Obstetricians and Gynecologists. Obstet Gynecol 2004;104:869–83.

Qazi G. Obstetric and perinatal outcome of multiple pregnancy. J Coll Physicians Surg Pak 2011;21:142–5.

47

Preterm birth

A 30-year-old African American woman, gravida 3, para 0, at 12 weeks of gestation comes to the office to discuss her risk of recurrent preterm delivery. The current pregnancy was conceived with the use of in vitro fertilization (IVF). During her first pregnancy, she gave birth at 28 weeks of gestation and during her second pregnancy she gave birth at 29 weeks of gestation; both following the spontaneous onset of preterm labor. She had a loop electrosurgical excision procedure performed before her first pregnancy. She smokes 10–15 cigarettes a day. The risk factor that is most strongly associated with a future preterm delivery is her

(A) non-Hispanic black race
(B) current IVF conception
* (C) obstetric history
(D) previous cervical surgery
(E) tobacco use

Many factors are associated with an increased risk of preterm delivery (Appendix C). A prior preterm birth is one of the strongest risk factors for recurrence and is associated with a twofold to fourfold increased risk above baseline. The number and gestational age of prior preterm births also significantly affect the risk of recurrence. Women with two consecutive spontaneous preterm deliveries have approximately a 40% risk of recurrence, but this risk increases to approximately 60% if both prior preterm births occurred before 32 weeks of gestation. Women with a recent preterm birth are at higher risk of recurrence than women with a remote preterm birth followed by a term delivery (Fig. 47-1).

Non-Hispanic black women have a 1.6-fold increased risk of preterm delivery compared with non-Hispanic white women and a 1.4-fold increased risk compared with Hispanic women. This racial disparity is even greater (2.0–2.4-fold) for very preterm births (less than 32 weeks of gestation). Non-Hispanic white women and Hispanic women have similar rates of preterm and very preterm birth.

Singleton pregnancies conceived by IVF have a twofold increased risk of premature birth compared with naturally conceived singleton pregnancies. The influence of a loop electrosurgical excision procedure on the preterm birth rate is controversial. A recent large cohort study reported a 2–3-fold increased risk of preterm delivery, whereas another large study found no effect. Several factors may affect this risk, including depth of excision, number of procedures, and interval from procedure to pregnancy. Tobacco use in pregnancy is associated with an increased risk of spontaneous preterm delivery. Women who smoke more than 10 cigarettes per day have a 1.5-fold risk compared with nonsmokers. Smoking cessation programs in

pregnancy are associated with a modest reduction in the rate of preterm birth. The participation of patients in such programs should be encouraged.

Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008;371:75–84.

Jackson RA, Gibson KA, Wu YW, Croughan MS. Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. Obstet Gynecol 2004;103:551–63.

Jakobsson M, Gissler M, Paavonen J, Tapper AM. Loop electrosurgical excision procedure and the risk for preterm birth. Obstet Gynecol 2009;114:504–10.

Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Mathews TJ, Osterman MJ. Births: final data for 2008. Natl Vital Stat Rep 2010;59:1–105.

McManemy J, Cooke E, Amon E, Leet T. Recurrence risk for preterm delivery. Am J Obstet Gynecol 2007;196:576.e1–6; discussion 576.e6–7.

Savitz DA, Murnane P. Behavioral influences on preterm birth: a review. Epidemiology 2010;21:291–9.

Werner CL, Lo JY, Heffernan T, Griffith WF, McIntire DD, Leveno KJ. Loop electrosurgical excision procedure and risk of preterm birth. Obstet Gynecol 2010;115:605–8.

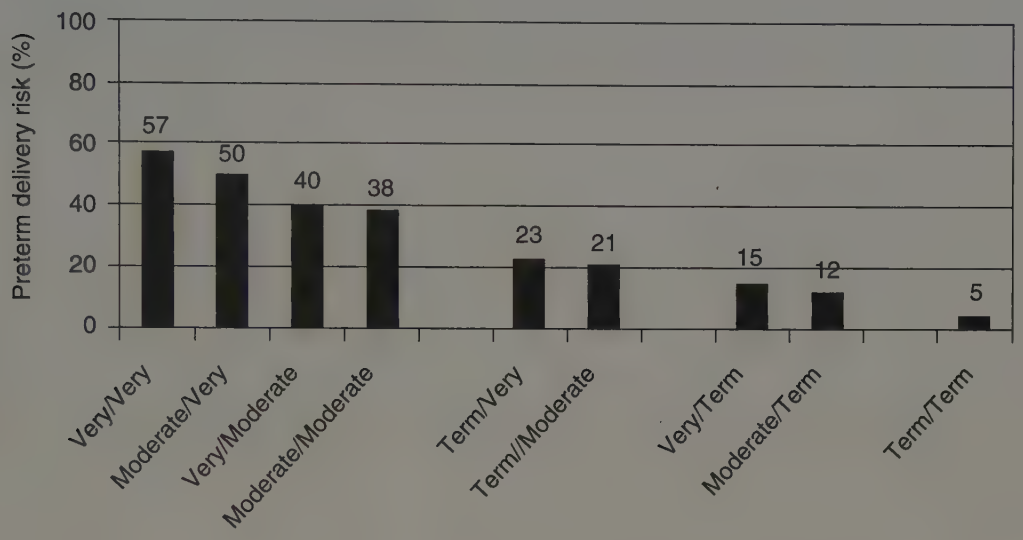


FIG. 47-1. Risk of preterm birth after two previous deliveries. Very = 21–31 weeks of gestation; Moderate = 32–36 weeks of gestation. Very/Moderate indicates a patient whose first delivery was very preterm (21–31 weeks of gestation) and second delivery was moderately preterm (32–36 weeks of gestation). (McManemy J, Cooke E, Amon E, Leet T. Recurrence risk for preterm delivery. Am J Obstet Gynecol 2007;196:576.e1–6.)

48

Fetal hyperthyroidism

A 38-year-old woman, gravida 1, at 36 weeks of gestation is noted to have a fetus with a fetal heart rate of 170 beats per minute (bpm) at a prenatal visit. She has chronic hypertension treated with nifedipine XL and a history of Graves disease treated with radioactive iodine 3 years ago. Her blood pressure is 138/82 mm Hg, her pulse is 78 bpm, and temperature is 37°C (98.6°F). Her abdomen and uterine fundus are nontender. She has a hematocrit of 36%, her blood type is A, and she is Rhesus positive. An antibody screen result reveals the presence of anti-Lewis antibodies. A urinalysis result shows trace protein and is otherwise negative. You perform a nonstress test and the result indicates a fetal heart rate of 180 bpm, minimal variability and no accelerations or decelerations, but with sustained baseline tachycardia. The most likely explanation for this fetal heart rate pattern is

(A) nifedipine
(B) chorioamnionitis
* (C) fetal hyperthyroidism
(D) isoimmunization
(E) preeclampsia

Thyroid disease is a common endocrine disorder in women of childbearing age. Maternal hyperthyroidism is present in approximately 0.2% of pregnancies and Graves disease accounts for 95% of these cases. Graves disease is an autoimmune disease where thyroid-stimulating immunoglobulins are produced. These immunoglobins act on the thyroid-stimulating hormone receptor to stimulate it.

Thyroid-stimulating immunoglobulin may cross the placenta. Fetal effects may occur after 20 weeks of gestation when the fetal thyroid can respond to stimuli. Although rare, fetal thyrotoxicosis is a risk in all women with a history of Graves disease. Fetal and neonatal Graves disease from transplacental thyroid-stimulating immunoglobulins may be unrelated to maternal thyroid function and may occur in women who are untreated, or have been treated with surgery or radioactive iodine. The effects of thyroid-stimulating immunoglobulins on the fetus may be attenuated by maternal treatment with antithyroid medication because these medications also cross the placenta.

Characteristics of fetal hyperthyroidism include fetal tachycardia (greater than 160 bpm), fetal goiter, advanced bone age, growth restriction, and craniosynostosis. Cardiac failure, hydrops, and stillbirth also have been reported. Fetal heart rate and fetal growth should be assessed in all fetuses of women with Graves disease. If fetal thyrotoxicosis is suspected, sonography to look for fetal goiter is indicated.

A normal-appearing fetal heart rate tracing except for a sustained baseline tachycardia should raise the suspicion of fetal hyperthyroidism, especially in a woman with a history of Graves disease. Fetal tachycardia may have other causes. Isoimmunization, leading to fetal anemia, may be associated with fetal tachycardia. However, anti-Lewis antibodies, which are immunoglobulin M and do not cross the placenta, do not cause isoimmunization. The described patient is afebrile, which makes chorioamnionitis unlikely. Stimulant drugs, such as terbutaline or cocaine, are associated with fetal tachycardia but nifedipine use is not. Preeclampsia may be associated with placental abruption, fetal hypoxemia, or fetal acidosis. In those cases, fetal tachycardia usually is accompanied by minimal or absent variability, recurrent decelerations, or both.

Management of intrapartum fetal heart rate tracings. Practice Bulletin No. 116. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:1232–40.

Peleg D, Cada S, Peleg A, Ben-Ami M. The relationship between maternal serum thyroid-stimulating immunoglobulin and fetal and neonatal thyrotoxicosis. Obstet Gynecol 2002;99:1040–3.

Thyroid disease in pregnancy. ACOG Practice Bulletin No. 32. American College of Obstetricians and Gynecologists; Obstet Gynecol 2002;100:387–96.

Towers CV, Thomas S, Steiger RM. The fetal heart monitor tracing in pregnancies complicated by fetal thyrotoxicosis. Am J Perinatol 2009;26:373–7.

49

Periodontal disease in pregnancy

A dentist reports that your patient, at 26 weeks of gestation, has moderate periodontal disease, gingivitis, and no cavities. The dentist would like to treat the periodontal disease with surgical scaling and root planing in an attempt to improve the patient's pregnancy outcome. The dentist believes that treatment can lower the patient's risk of preterm birth. The patient had a medically indicated preterm birth at 35 weeks of gestation in her last pregnancy after a motor vehicle collision. Treatment of periodontal disease in the second trimester would most likely reduce the risk of

(A) preterm birth
(B) preeclampsia
(C) fetal growth restriction
* (D) maternal tooth loss

Periodontal disease is common in pregnancy and is associated with preterm birth. Some have suggested that it could play a causal role in early delivery. However, randomized controlled trials have shown that treatment of periodontal disease in pregnancy does not reduce the risk of spontaneous preterm birth. Moreover, the described scenario depicts a previous medically indicated preterm birth that is unlikely to increase the risk of recurrence in this pregnancy.

Periodontal disease represents an important maternal health concern. It causes tooth loss and the need for treatment during pregnancy to improve maternal oral health. Oral hygiene is a part of a woman's overall health maintenance in the prenatal period and pregnancy should not delay indicated dental care. Preventive services and treatment for acute problems should be recommended.

Patients and their dentists often are hesitant to treat diseases of the mouth in pregnancy. Delay of treatment can cause long-term oral health problems. Local anesthetics, dental X-rays, surgical procedures in the mouth, and antibiotic therapy are safe in pregnancy. Often the obstetrician will need to encourage his or her dental colleagues to provide indicated treatments.

The condition of a mother's dentition is highly correlated with oral health in her children. Some data suggest that pregnancy provides a teachable moment for health behaviors. Encouraging good oral health practices such as brushing, flossing, and periodic examinations may favorably influence the teeth of the next generation.

The described case highlights a useful principle for health care providers who advise mothers-to-be about health behaviors. Types of behavior that are generally thought to be beneficial in nonpregnant reproductive-aged women are infrequently harmful in pregnancy. Therefore, unless a behavior is specifically known to be harmful in pregnancy, your advice should be to maintain that behavior during the patient's pregnancy.

Albert DA, Begg MD, Andrews HF, Williams SZ, Ward A, Conicella ML, et al. An examination of periodontal treatment, dental care, and pregnancy outcomes in an insured population in the United States. Am J Public Health 2011;101:151–6.

Kloetzel MK, Huebner CE, Milgrom P. Referrals for dental care during pregnancy. J Midwifery Womens Health 2011;56:110–7.

Macones G. Treatment of periodontal disease in pregnancy. BMJ 2010; 341:c7090.

Matevosyan NR. Periodontal disease and perinatal outcomes. Arch Gynecol Obstet 2011;283:675–86

Polyzos NP, Polyzos IP, Zavos A, Valachis A, Mauri D, Papanikolaou EG, et al. Obstetric outcomes after treatment of periodontal disease during pregnancy: systematic review and meta-analysis. BMJ 2010;341:c7017.

Wilkinson SA, Miller YD, Watson B. The effects of a woman-focused, woman-held resource on preventive health behaviors during pregnancy: the pregnancy pocketbook. Women Health 2010;50:342–58.

50

Motor vehicle collision

A 27-year-old primigravid woman at 32 weeks of gestation is transported to the emergency department following a motor vehicle collision. She was the restrained driver of a vehicle that was struck at approximately 48 km/h (30 mph). She was wearing her seat belt below the uterine fundus and across her hips. Her car's air bags deployed in the collision. On initial evaluation, her abdomen is gravid with a fundal height of 31 cm. The abdomen is tender to palpation throughout. Pelvic examination reveals no vaginal bleeding; the cervix is closed and long. Ultrasonography shows a singleton gestation in cephalic presentation with normal amniotic fluid volume and a normal-appearing posterior placenta. Fetal heart tracing shows a baseline of 130 beats per minute without decelerations. Uterine monitoring shows uterine contractions every 20–25 minutes. Kleihauer-Betke testing is normal and her blood type is O positive. The factor in this case that most strongly indicates the need for prolonged observation and monitoring is

* (A) abdominal tenderness
(B) air bag deployment
(C) posterior placental location
(D) use of seat belt
(E) uterine contractions

The leading cause of death in females aged 6–29 years is motor vehicle collisions. Women are also more likely than men to be involved in a collision per 10 million miles driven. Up to 3% of pregnancies may be complicated by automobile collisions. The added vulnerability of a fetus in utero prompts careful attention to any pregnant woman involved in an automobile collision.

During the initial assessment of a gravid patient following trauma, the presence of frequent uterine contractions, vaginal bleeding, abdominal or uterine tenderness (even if slight), postural hypotension, or fetal heart rate abnormalities should prompt increased clinical concern for placental abruption. The minimum observation period recommended is 4 hours, but a low threshold to extend observation to 24 hours or longer should be maintained, especially in the presence of any of the aforementioned symptoms.

Air bags were initially developed to safeguard a 81.7 kg (180 lb) male driver and were not evaluated for women. Later standards adopted by the National Highway Traffic Safety Administration for advanced air bags require that these safety measures protect women and children. A small review of pregnant women in motor vehicle collisions that involved air bag deployment did not show an increase in risk of placental abruption. Ideally, there should be a 25.4-cm (10-in.) separation between an air bag and the sternum of the pregnant patient.

Although posterior placentation may theoretically increase the chance of a deceleration–rebound injury pattern and, therefore, shear injury causing abruption, to date, no studies have examined the effect of placental location on the probability of abruption after automobile collisions.

Proper seat belt use in pregnancy has been associated with a decrease in maternal morbidity and mortality. Unfortunately, many patients do not consistently use seat belts in the correct fashion. Approximately 25% of pregnant patients do not wear seat belts, and 25–50% do not know how to wear seat belts correctly during pregnancy. Indeed, in one study, two thirds of pregnant patients did not receive any guidance regarding the proper use of seat belts during pregnancy. The shoulder belt should be placed over the clavicle and between the breasts. The lap belt should ride below the gravid abdomen, across the hips and upper thighs. Adverse fetal outcomes are most strongly associated with crash severity, severe maternal injury, and incorrect seat belt use.

Increased presence of infrequent uterine contractions on postcollision monitoring does not necessarily predict the presence of abruption. Fewer than six contractions per hour in the first 4 hours of monitoring combined with normal fetal heart rate monitoring is unlikely to be associated with delayed abruption. If contractions are more frequent, or are associated with vaginal bleeding, abdominal pain or tenderness, uterine irritability, or nonreassuring fetal heart rate patterns, prolonged monitoring should be considered. Typically, 83% of patients will be discharged from the hospital still pregnant.

Laboratory evaluation in pregnant collision victims should include consideration of an assessment of mater-

nal hemoglobin, coagulation profile, blood typing and Rhesus group, Kleihauer-Betke testing (or an appropriate alternative), and toxicology studies. Because the Kleihauer-Betke test does not detect very small feto–maternal hemorrhages, consideration should be given to prophylactic doses of Rho (D) immune globulin in all Rh-negative pregnant women involved in automobile collisions.

Brown HL. Trauma in pregnancy. Obstet Gynecol 2009;114:147–60.

El Kady D. Perinatal outcomes of traumatic injuries during pregnancy. Clin Obstet Gynecol 2007;50:582–91.

Klinich KD, Flannagan CA, Rupp JD, Sochor M, Schneider LW, Pearlman MD. Fetal outcome in motor–vehicle crashes: effects of crash characteristics and maternal restraint. Am J Obstet Gynecol 2008;198:450.e1–9.

McGwin G Jr, Willey P, Ware A, Kohler C, Kirby T, Rue LW, 3rd. A focused educational intervention can promote the proper application of seat belts during pregnancy. J Trauma 2004;56:1016–21.

51

Gestational diabetes mellitus recurrence

A 38-year-old African American woman, gravida 3, para 2, with a body mass index (calculated as weight in kilograms divided by height in meters squared [kg/m^2]) (BMI) of 34 returns to your office for prenatal care at 18 weeks of gestation. Her previous pregnancy 3 years ago was complicated by a diagnosis of gestational diabetes mellitus. In that pregnancy, she eventually required insulin therapy to control her blood sugar. She discontinued the insulin after giving birth to a 3.9-kg infant. Since that delivery, she has avoided desserts and takes a daily 45-minute walk. She had a negative screen result in the postpartum period and a normal 50-g glucose tolerance test in the first trimester. The best next step in management is to

(A) perform a 50-g glucose tolerance test now
* (B) perform a 50-g glucose tolerance test at 26 weeks of gestation
(C) initiate a very low carbohydrate diet (less than 30 g/day)
(D) initiate empiric metformin therapy
(E) perform urinary glucose screening test

The rate of gestational diabetes mellitus in the general obstetric population ranges from 1% to 14%, although women with a history of gestational diabetes mellitus in a prior pregnancy have a 30–80% risk of recurrence in their next pregnancy. Women with no such history in a prior pregnancy have a risk of gestational diabetes mellitus of approximately 1%. Risk factors and pathophysiology of gestational diabetes parallel those found in type 2 diabetes and, therefore, would be likely to persist or recur in future pregnancies. The variation in published gestational diabetes recurrence rates is because of the differences in percentage of high-risk racial and ethnic groups, and obesity rates in the studied populations. Additionally, the intensity of postpartum glucose testing to diagnose those with persistent hyperglycemia and re-label them as having type 2 diabetes mellitus will diminish the pool of potential women with gestational diabetes in the next pregnancy. Consequently, some recurrences of gestational diabetes likely represent persistence of abnormal glucose metabolism in the interpregnancy interval.

Non-Hispanic white women tend to have rates of recurrence less than 40%. African American women, Latin American women, and Asian American women have recurrence rates greater than 50%. Other risk factors for recurrence of gestational diabetes mellitus include obesity, older maternal age, earlier diagnosis in prior pregnancy, family history of type 2 diabetes, and the need for insulin in prior pregnancy. These risk factors also increase the risk of type 2 diabetes in later years. Weight gain between pregnancies and short interval pregnancy are additional risk factors for recurrent gestational diabetes.

Because these risk factors are not consistently predictive of gestational diabetes recurrence (or their absence indicate a lack of recurrence), women should be rescreened in future pregnancies. Additionally, postpartum screening after the index pregnancy also may allow correct diagnosis of preexisting type 2 diabetes and more optimal preconceptional management for the next pregnancy. The hormonal changes in pregnancy that cause insulin resistance should revert to normal levels quickly in the postpartum period, but approximately 10% of women will continue to have postpartum glucose intolerance if they are checked.

Ideally, interpregnancy intervention with lifestyle changes for modifiable risk factors, such as obesity, might potentially decrease gestational diabetes risks in later

pregnancies as well as type 2 diabetes risk in later life. Breastfeeding may affect development of metabolic syndrome in the mother. In research settings, pharmacologic interventions, such as administration of troglitazone, have been used to attempt to preserve beta cell function in women who had gestational diabetes mellitus. Routine islet autoantibody testing is not recommended postpartum and no genetic testing for risk of later type 2 diabetes is available.

Pregnancies with diabetes detected at less than 24 weeks of gestation are noted to have worse glucose tolerance, higher risk of hypertensive complications, intrauterine fetal demise, and neonatal hypoglycemia. Therefore, recommendations suggest early screening in high-risk women, such as those with prior gestational diabetes, as soon as is practical to ameliorate the consequences of early gestational diabetes. If the result of a glucose screening with a 50-g glucose tolerance test is negative in early pregnancy, the recommended practice is to perform repeat testing in the third trimester as in other pregnancies. This patient should be rescreened at 26 weeks of gestation.

Efforts to prevent gestational diabetes mellitus with high fiber diets in pregnancy have not demonstrated efficacy. Small trials of pregnant women who have eaten foods that have a low glycemic index have suggested there may be an effect on large for gestational age birth weight rates. Very low carbohydrate diets that induce ketone formation have not been recommended in pregnancy. A urinary glucose screening test would not be appropriate for the described patient at this time. Similarly, initiation of metformin therapy without a diagnosis would not be the best next step for this patient.

Hedderson MM, Williams MA, Holt VL, Weiss NS, Ferrara A. Body mass index and weight gain prior to pregnancy and risk of gestational diabetes mellitus. Am J Obstet Gynecol 2008;198:409.e1–7.

Kim C, Berger DK, Chamany S. Recurrence of gestational diabetes mellitus: a systematic review. Diabetes Care 2007;30:1314–9.

Metzger BE, Buchanan TA, Coustan DR, de Leiva A, Dunger DB, Hadden DR, et al. Summary and recommendations of the Fifth International Workshop–Conference on Gestational Diabetes Mellitus [published erratum appears in Diabetes Care 2007;30:3154]. Diabetes Care 2007;30(suppl 2):S251–60.

Nohira T, Kim S, Nakai H, Okabe K, Nohira T, Yoneyama K. Recurrence of gestational diabetes mellitus: rates and risk factors from initial GDM and one abnormal GTT value. Diabetes Res Clin Pract 2006;71:75–81.

Screening and diagnosis of gestational diabetes mellitus. Committee Opinion No. 504. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:751–3.

Tieu J, Crowther CA, Middleton P. Dietary advice in pregnancy for preventing gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD006674. DOI: 10.1002/14651858.CD006674.pub2.

Verier-Mine O. Outcomes in women with a history of gestational diabetes. Screening and prevention of type 2 diabetes. Literature review. Diabetes Metab 2010;36:595–616.

Xiang AH, Peters RK, Kjos SL, Marroquin A, Goico J, Ochoa C, et al. Effect of pioglitazone on pancreatic beta-cell function and diabetes risk in Hispanic women with prior gestational diabetes. Diabetes 2006;55:517–22.

52

Autoimmune disorders and pregnancy

A 23-year-old primigravid woman presents to your office at 20 weeks of gestation with fatigue, photophobia, a rash on her face, and new onset pain in several metatarsal joints and her wrist. Her blood pressure is 130/80 mm Hg and she has new onset 1+ proteinuria. On physical examination, her painful metatarsal joints appear to be swollen. The most likely diagnosis is

(A) Sjögren syndrome
* (B) systemic lupus erythematosus (SLE)
(C) carpal tunnel syndrome
(D) rheumatoid arthritis
(E) osteoarthritis

The most likely diagnosis is SLE. The American College of Rheumatology has devised a classification system that includes 11 criteria for SLE (Box 52-1). In order for a patient to be diagnosed with SLE, the individual must meet four of the 11 criteria. This classification system was devised to include patients in clinical trials and research studies but often is used as diagnostic criteria for the disease. Early in the disease, a patient may not meet all four criteria.

Systemic lupus erythematosus is a chronic inflammatory autoimmune disorder that primarily affects women in the third and fourth decade of life. African Americans and Hispanics have a much higher incidence of the disease than whites. The incidence of the disease is higher if a first-degree family member is affected and if associated with specific human leukocyte antigen haplotypes, specifically DR2 and DR3 and null complement alleles.

BOX 52-1

Revised Criteria for the Classification of Systemic Lupus Erythematosus

- Malar rash
- Discoid rash
- Photosensitivity
- Oral ulcers, usually painless
- Arthritis: nonerosive arthritis of 2 or more joints, characterized by swelling, effusion, and tenderness
- Serositis: pleuritis or pericarditis
- Renal disorder: persistent proteinuria or cellular cast
- Neurologic disorder: seizures or psychosis
- Hematologic disorder: hemolytic anemia, leukopenia, lymphopenia, or thrombocytopenia
- Immunologic disorder: anti-dsDNA, anti-Sm, or false-positive serologic test for syphilis
- Antinuclear antibody titer

Abbreviations: anti-dsDNA, anti–double stranded DNA antibodies; anti-Sm, anti-Smith antibodies.

Petri M. Review of classification criteria for systemic lupus erythematosus. Rheum Dis Clin North Am 2005;31:245–54, vi. Copyright 2005 by Elsevier.

Patients with SLE may present with an array of symptoms. The most common symptoms are constitutional, dermatologic, and musculoskeletal. Other systems may be involved, such as the central nervous system, or the cardiopulmonary, renal, or hematologic systems. The most common autoantibodies present with SLE are antinuclear antibodies and anti–double-stranded DNA. These autoantibodies are sensitive but not specific. Most patients with SLE are positive for these autoantibodies. However, many patients who have these autoantibodies may not have SLE. The obstetrician should recognize SLE and refer the patient to the appropriate specialist. The disease should be treated early and effectively to prevent end organ damage.

Rheumatoid arthritis is an autoimmune disorder more commonly seen in women than in men. The onset of the disease usually occurs later in life than SLE, predominantly in the fourth and fifth decades. The disease presents primarily with insidious joint pain. The joints most often affected are the proximal interphalangeal, metacarpophalangeal, metatarsophalangeal joints, wrists, knees, and ankles. The facial rash and new onset proteinuria in the described patient are more consistent with SLE than rheumatoid arthritis. Autoantibodies most consistent with rheumatoid arthritis are rheumatoid factor and cyclic citrullinated peptides.

Sjögren syndrome is characterized by dry eyes and mouth; it can be a primary diagnosis or associated with other autoimmune disorders, such as rheumatoid arthritis. As with SLE and rheumatoid arthritis, this disorder is much more common in women and usually presents in the fifth to seventh decades of life. Common autoantibodies associated with Sjögren syndrome are rheumatoid

factor and antinuclear antibodies. Anti-SS-A and anti-SS-B are present if Sjögren syndrome is the primary diagnosis but also may be present in lupus patients.

Carpal tunnel syndrome is common in pregnancy and presents as pain and paresthesia in the first three fingers. The symptoms can be bilateral and most often occur in the third trimester. The pain usually is worse at night and can be exacerbated by repetitive motions of the wrist during the day. The patient with carpal tunnel syndrome generally does not complain of other systemic problems. The use of wrist splints at night can lessen the pain in most patients and the symptoms usually resolve within 2 weeks postpartum.

Osteoarthritis is mainly a disease that affects older individuals. The most common characteristic of the disease is joint pain relieved by rest. Inflammation in the joints is minimal, if present at all. Obesity is a risk factor. Systemic symptoms are absent in comparison with the arthritis caused by autoimmune disease.

Bagavant H, Fu SM. Pathogenesis of kidney disease in systemic lupus erythematosus. Curr Opin Rheumatol 2009;21:489–94.

Borg-Stein J, Dugan SA, Gruber J. Musculoskeletal aspects of pregnancy. Am J Phys Med Rehabil 2005;84:180–92.

Coletta J, Simpson LL. Maternal medical disease and stillbirth. Clin Obstet Gynecol 2010;53:607–16.

Marker-Hermann E, Fischer-Betz R. Rheumatic diseases and pregnancy. Curr Opin Obstet Gynecol 2010;22:458–65.

Petri M. Review of classification criteria for systemic lupus erythematosus. Rheum Dis Clin North Am 2005;31:245–54, vi.

Trethewey P. Systemic lupus erythematosus. Dimens Crit Care Nurs 2004;23:111–5.

53

Diagnosis of parvovirus

A 29-year-old woman, gravida 2, para 1, comes to see you for an urgent prenatal visit at 19 weeks of gestation. She is a teacher at an elementary school. In the past week, two children in her class have been diagnosed with parvovirus infection. The woman feels well, has had no rash or systemic symptoms, and does not have a fever. Parvovirus serology reveals negative immunoglobulin G (IgG) and immunoglobulin M (IgM) antibody titers. With regard to concerns related to parvovirus testing, the most appropriate next step is

* (A) repeat parvovirus antibody serology in 2–4 weeks
(B) parvovirus DNA polymerase chain reaction (PCR) testing
(C) detailed fetal anatomic survey
(D) serial fetal middle cerebral artery Doppler velocimetry

Parvovirus is a single-stranded DNA virus transmitted via respiratory droplets. Approximately 20–30% of patients are asymptomatic but the typical course is a low-grade fever, arthralgia, and fatigue sometimes associated with a "slapped cheek" rash on the face, trunk, and extremities. In rare cases, this may be followed by myocarditis or a transient aplastic crisis. Susceptible or nonimmune patients have a 25% risk of acquiring the infection after exposure.

The major fetal risk with parvovirus infection is aplastic crisis, causing anemia, which can lead to hydrops fetalis. Myocarditis is a rarer fetal complication. Vertical transmission to the fetus occurs in 30% of affected mothers. Risk of hydrops is higher with fetal infections that occur earlier in pregnancy, with a 10% risk before 20 weeks of gestation and a 5% risk after 20 weeks of gestation. Hydrops fetalis is associated with a fetal loss rate as high as 30–50% if not treated. Treatment for fetal anemia in these cases is intrauterine transfusion. There is no risk of congenital abnormalities related to parvovirus infection in the first trimester.

Maternal diagnosis of parvovirus infection relies on antibody serology. Although IgM antibodies usually are detected within 3 days of symptoms, if present, they disappear typically after 30–60 days but may persist up to 120 days in some cases. By contrast, IgG antibodies present 7 days after symptoms, if present, and persist for life.

Pregnant patients with unknown immunity status who are exposed to parvovirus should be tested for IgM and IgG antibodies. The presence of IgG antibodies alone indicates immunity, whereas the presence of both IgM and IgG antibodies indicates that infection occurred between 1 week and 6 months before testing. As a result, exposed patients with both antibodies should be evaluated as if recently infected. Absence of antibodies suggests that the patient has not been infected, and is susceptible, or that the testing was done too early in the disease process. Given this, and that 20–30% of patients who become seropositive do not have symptoms, testing for the described patient should be repeated 2–4 weeks later.

If seroconversion is documented, or if there is a strong clinical suspicion of parvovirus infection, weekly assessment for hydrops and signs of anemia is warranted. This typically is performed up to 10 weeks from the time of exposure or infection. Anemia is assessed with middle cerebral artery Doppler velocimetry, specifically looking for elevated peak systolic velocity values. Amniotic fluid PCR testing can definitively diagnose parvovirus infection, particularly hydrops of unknown etiology, but should not be used because of its invasiveness if maternal seroconversion does not occur. In the described case scenario, PCR testing, ultrasonography, or middle cerebral artery Doppler velocimetry could be considered after maternal infection is confirmed.

American College of Obstetricians and Gynecologists. Perinatal viral and parasitic infections. ACOG Practice Bulletin 20. Washington, DC: ACOG; 2000.

Cosmi E, Mari G, Delle Chiaie L, Detti L, Akiyama M, Murphy J, et al. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia resulting from parvovirus infection. Am J Obstet Gynecol 2002;187:1290–3.

Enders M, Weidner A, Zoellner I, Searle K, Enders G. Fetal morbidity and mortality after acute human parvovirus B19 infection in pregnancy: prospective evaluation of 1018 cases. Prenat Diagn 2004;24:513–8.

Markenson GR, Yancey MK. Parvovirus B19 infections in pregnancy. Semin Perinatol 1998;22:309–17.

Rodis JF, Quinn DL, Gary GW Jr, Anderson LJ, Rosengren S, Cartter ML, et al. Management and outcomes of pregnancies complicated by human B19 parvovirus infection: a prospective study. Am J Obstet Gynecol 1990;163:1168–71.

54

Tuberculosis

A 30-year-old woman, gravida 3, para 2, at 8 weeks of gestation visits your office for prenatal care. She immigrated to the United States from Central America 6 months ago. She reports that she was vaccinated with the bacille Calmette-Guérin (BCG) vaccine as a child. She has had no cough, night sweats, or weight loss. She is human immunodeficiency virus (HIV) negative. The best option for tuberculosis (TB) screening in this woman is

* (A) tuberculin skin testing
(B) chest X-ray with abdominal shield
(C) three first-morning sputums
(D) induced sputum for acid-fast bacilli stain
(E) observation for development of symptoms

Approximately 19–43% of the world's population is infected with *Mycobacterium tuberculosis*. Worldwide, TB is a leading cause of nonobstetric mortality in women of childbearing age. Although overall rates of tuberculosis B have decreased in the United States, recent immigrants remain a source of new infections, and individuals who immigrated in the past 5 years are at highest risk of infection. Co-infection with HIV and multidrug-resistant TB are added challenges to the goal of eradication of the disease.

Generally *M tuberculosis* infects people through contact with respiratory droplets. Most healthy adults' immune systems will contain the infection and it will become latent. The bacteria remain alive and capable of initiating active disease, particularly in situations of stress and immune compromise. Initial symptoms of active disease are nonspecific: cough, fatigue, fever, malaise, night sweats, and weight loss. Pregnancy, on its own, has not been associated with an increased risk of acquiring tuberculosis or of developing active disease.

In locations of high incidence of the disease, BCG vaccine, a live attenuated vaccine, is administered in children to prevent disseminated TB. The vaccine is not completely effective. It may not confer protection against pulmonary TB nor may it be efficacious in adults. The vaccine's benefits tend to wane over a decade. Improved methods of TB prevention are a public health priority.

In patients suspected of having active tubercular disease, chest X-ray followed by microscopic identification of acid-fast bacilli in sputum or culture remains the criterion standard of diagnosis. Use of enhanced microscopic techniques and polymerase chain reaction assays specific for *M tuberculosis* are improving sensitivity and specificity of diagnostic algorithms.

Individuals with latent infection who have immigrated to the United States constitute a reservoir for future active infection. Improvement of diagnostic techniques to identify individuals with latent TB remains a public health priority. The Mantoux tuberculin skin test is the most commonly used diagnostic method. An intradermal injection of 0.1 mL of tubercular extract purified protein derivative (PPD) is given and the area of induration (read perpendicular to long axis of forearm), not redness, is checked 48–72 hours later (Table 54-1). There are few contraindications to the Mantoux skin test—only a prior severe reaction is considered as a reason to avoid testing. False-negative test results can occur because of an anergy associated with immune compromise and such test results have been reported with concurrent administration of live attenuated vaccines. Anergy panels can assist with interpretation of skin testing in immune compromised individuals but generally are not used for TB screening in HIV-infected individuals.

Prior BCG vaccination is not considered a contraindication to skin testing. Because BCG is administered in locations with a high incidence of TB, testing may be particularly important in this group. Although a positive skin test result may be due to previous vaccination, these patients are managed as if infected (Table 54-1). If the skin reaction is negative in a high-risk patient, a second skin test is administered 2–3 weeks later to improve sensitivity. Older tubercular tine tests are not as sensitive. Interferon gamma assays on peripheral blood T-cells incubated with PPD are used in some clinical settings as an alternative to Mantoux skin testing. Although the validity in pregnancy of interferon gamma assays on peripheral blood T-cells incubated with PPD is unknown, it may be a useful adjunct to testing.

For individuals with positive Mantoux skin tests, a chest X-ray is performed to rule out active pulmonary TB because the chest is the most common location of active disease. In pregnancy, chest X-ray can be performed in any trimester using a lead shield over the pelvis.

Treatment of active TB disease in pregnant women should not be delayed and, with a few adjustments, should be similar to treatment outside of pregnancy. An

TABLE 54-1. Classification of the Tuberculin Skin Test Reaction

A Positive Test Result for Those With an Induration of 5 mm or More	A Positive Test Result for Those With an Induration of 10 mm or More	A Positive Test Result for Those With an Induration of 15 mm or More
• HIV-infected individuals • A recent contact of an individual with TB disease • Individuals with fibrotic changes on chest radiograph consistent with prior TB • Patients with organ transplants • Individuals who are immunosuppressed for other reasons (eg, taking the equivalent of greater than 15 mg/day of prednisone for 1 month or longer, taking TNF-α antagonists)	• Recent immigrants (within 5 years) from high-prevalence countries • Injection drug users • Residents and employees of high-risk congregate settings • Mycobacteriology laboratory personnel • Individuals with clinical conditions that place them at high risk • Children younger than 4 years of age • Infants, children, and adolescents exposed to adults in high-risk categories	• Any individual, including individuals with no known risk factors for TB. • However, targeted skin testing programs should only be conducted among high-risk groups.

Abbreviations: TB, tuberculosis; TNF-α, tumor necrosis factor-alpha.

Centers for Disease Control and Prevention. Tuberculin Skin Testing. Available at http://www.cdc.gov/tb/publications/factsheets/testing/skintesting.htm. Accessed September 1, 2011.

exception is streptomycin treatment, which should be avoided as it can be associated with fetal ototoxicity. For latent TB infection, isoniazid prophylaxis (administered with pyridoxine) for 6–9 months is recommended. Isoniazid hepatotoxicity has been reported in pregnant and nonpregnant patients. Recommendations regarding the timing of initiation of isoniazid prophylaxis during pregnancy or the postpartum period remain under discussion.

Carbillon L, Uzan M, Uzan S. Pregnancy, vascular tone, and maternal hemodynamics: a crucial adaptation. Obstet Gynecol Surv 2000; 55:574–81.

Carlin A, Alfirevic Z. Physiological changes of pregnancy and monitoring. Best Pract Res Clin Obstet Gynaecol 2008;22:801–23.

Mendelson MA. Pregnancy in the woman with preexisting cardiovascular disease. In: Global library for women's medicine. London: Foundation for the Global Library for Women's Medicine; 2008. Available at: http://www.glowm.com/?p=glowm.cml/section_view&articleid=161. Retrieved June 11, 2012.

Moghbeli N, Pare E, Webb G. Practical assessment of maternal cardiovascular risk in pregnancy. Congenit Heart Dis 2008;3:308–16.

Reimold SC, Rutherford JD. Clinical practice. Valvular heart disease in pregnancy. N Engl J Med 2003;349:52–9.

55

Hospital standards for neonatal resuscitation

A patient is admitted in preterm labor at 23 weeks of gestation with advanced cervical dilatation of 4 cm. The hospital in which you are caring for this patient does not resuscitate babies who are born before 24 weeks of gestation, whereas the other hospital across town does resuscitate babies who are born at or after 22 weeks of gestation. The patient has done internet research and is aware of the latter hospital's policy. She requests transfer as she wants "everything done" on behalf of her unborn child. After checking with the other hospital, conditions will allow her transport. In addition to neonatal consultation, the best next step in her management should be

* (A) maternal transport
(B) neonatal transport
(C) legal consultation
(D) ethics committee consultation

The ethical concept of maternal autonomy specifies that a family's reasonable wishes should be respected and responded to in regard to the care of their newborn infant, even at the extremes of prematurity. With a mentally competent adult, maternal wishes should be respected, and acted upon, if they can be done so safely. Given that practice regarding neonatal resuscitation varies among hospitals, it is not uncommon for perinatal units within the same geographic area to have different policies. The hospital across town has practices that are more consistent with the patient's informed wishes and maternal transport is indicated. The obstetrician who cares for a mother whose fetus has a gestational age at the borderline of viability should be aware of practices within their hospital and in other perinatal units in their geographic area. Large observational studies suggest that maternal transport is associated with better perinatal outcomes when compared with neonatal transport. In this scenario, neonatal transport might likely be impossible because a decision to not resuscitate a newborn this preterm most often results in death. Transfer of patients from hospital to hospital requires contacting the receiving institution, informing them of the clinical situation, confirming they have adequate capacity in labor and delivery and the neonatal intensive care unit to care for mother and baby, and receiving their permission. The Emergency Medical Treatment and Active Labor Act requires that these and other prerequisites be met before transfer.

If the transferring health care provider will not be caring for his or her patient in the receiving hospital, he or she should contact the receiving health care provider. The health care provider will need to transmit not only facts about the patient's condition(s), but the summary of their discussions and the mother's wishes. Likewise, a conversation between nurses in the receiving and sending hospitals will facilitate communication.

Health care providers must carefully examine their own biases in these difficult situations. Although it is reasonable to express one's opinion when asked, great care must be exercised to avoid using one's influence to push the patient in one direction or another. Sometimes the conclusions drawn by an informed patient's conscience will conflict with conventional wisdom and, if medically safe, second opinions or maternal transfer will need to be considered.

Before maternal transport and in light of the receiving hospital's resuscitation policies, it would be reasonable to initiate secondary prevention treatments to prevent the sequelae of extreme prematurity. Such possible treatments would include corticosteroids and magnesium sulfate, which could serve to slow uterine contractions temporarily to facilitate transport.

Abdel-Latif ME, Bajuk B, Oei J, Vincent T, Sutton L, Lui K. Does rural or urban residence make a difference to neonatal outcome in premature birth? A regional study in Australia. NICUS Group [published erratum appears Arch Dis Child Fetal Neonatal Ed 2006;91:F390]. Arch Dis Child Fetal Neonatal Ed 2006;91:F251–6.

Caliendo C, Millbauer L, Moore B, Kitchen E. Obstetric triage & EMTALA regulations. Practice strategies for labor and delivery nursing units. AWHONN Lifelines 2004;8:442–8.

Finer N, Rich W. Neonatal resuscitation for the preterm infant: evidence versus practice. J Perinatol 2010;30 Suppl:S57–66.

Mann RJ. The interface between legal and ethical issues in reproductive health. J Midwifery Womens Health 2004;49:182–7.

Teshome G, Closson FT. Emergency Medical Treatment and Labor Act: the basics and other medicolegal concerns. Pediatr Clin North Am 2006;53:139–55, vii.

56
Oligohydramnios

A 29-year-old woman, gravida 2, para 0, presents at 37 weeks of gestation with decreased fetal movement for 8 hours. The pregnancy has been uncomplicated to date. The nonstress test is reactive, but several brief variable decelerations are present. In order to assess her amniotic fluid (AF) volume, the most appropriate test is

(A) AF index
* (B) single deepest pocket
(C) three-dimensional ultrasonography
(D) two-diameter pocket technique

Normal AF volume is essential for fetal growth and development as well as protection of the fetus and umbilical cord. Oligohydramnios, or diminished AF volume, is variably associated with fetal anomalies, postterm pregnancy, fetal growth restriction, preeclampsia, cesarean delivery for abnormal fetal heart tracing, umbilical cord compression, meconium-stained fluid, and low Apgar scores.

Dye-dilution studies and collection of AF at the time of cesarean delivery are the most accurate means to measure AF volume, but they are invasive and impractical. Ultrasonography is currently by far the most common means used to assess AF volume. Several techniques have been described, but all poorly predict low AF volume. Furthermore, the two most commonly reported tests, amniotic fluid index (AFI) and single deepest pocket, correlate poorly with peripartum complications (eg, cesarean delivery for abnormal fetal heart rate tracing, low Apgar scores, and neonatal acidemia).

The single deepest pocket technique involves measuring the largest vertical pocket of fluid, excluding umbilical cord or fetal parts, with a horizontal measurement of at least 1 cm at a right angle to the uterine contour. A depth of less than 2 cm is classically defined as oligohydramnios. Amniotic fluid index is determined by dividing the uterus into four quadrants. The linea nigra is divided into right and left quadrants and the umbilicus is divided into upper and lower quadrants. The maximum vertical depth of amniotic fluid in each quadrant, without cord or fetal extremities, is measured in centimeters and summed. An AFI of 5 cm or less is considered to indicate oligohydramnios. The 2-diameter pocket technique involves multiplying the vertical depth by the horizontal diameter of the largest pocket of amniotic fluid, excluding the umbilical cord. A value of 0–15 cm^2 is an indication of oligohydramnios. This option is reported less frequently in the literature than AFI and single deepest pocket. Limited data show that three-dimensional ultrasonography correlates well with more standard two-dimensional techniques. The need for appropriate equipment and knowledge to perform three-dimensional ultrasonography limits its utility.

Compared with the single deepest pocket technique, a recent Cochrane meta-analysis of five randomized trials reported that AFI was associated with significantly more cases of oligohydramnios, labor induction, and cesarean delivery for abnormal fetal heart tracing. The two techniques were found to be similar in regard to peripartum outcomes, including admission to a neonatal intensive care unit, an umbilical artery pH of less than 7.1, the presence of meconium, an Apgar score of less than 7 at 5 minutes, and cesarean delivery. The single deepest pocket measurement appears to be the better option because the use of AFI increases the rate of diagnosis of oligohydramnios and the rate of induction of labor without improvement in outcome.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. ACOG Practice Bulletin 9. Washington, DC: ACOG; 1999.

Chauhan SP, Doherty DD, Magann EF, Cahanding F, Moreno F, Klausen JH. Amniotic fluid index vs single deepest pocket technique during modified biophysical profile: a randomized clinical trial. Am J Obstet Gynecol 2004;191:661–7; discussion 667–8.

Magann EF, Sanderson M, Martin JN, Chauhan S. The amniotic fluid index, single deepest pocket, and two-diameter pocket in normal human pregnancy. Am J Obstet Gynecol 2000;182:1581–8.

Nabhan AF, Abdelmoula YA. Amniotic fluid index versus single deepest vertical pocket as a screening test for preventing adverse pregnancy outcome. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD006593. DOI: 10.1002/14651858.CD006593.pub2.

57

Influenza vaccination

A pregnant patient at 8 weeks of gestation comes to your office during the influenza season and inquires about influenza vaccination. She would like to receive the vaccine if you feel it is safe for her to receive it. She is afraid of injections and prefers the nasal spray administration route. As her physician you inform her that she should receive

(A) nasal spray vaccine after 12 weeks of gestation
(B) injectable vaccine after 12 weeks of gestation
* (C) injectable vaccine today
(D) nasal spray vaccine today
(E) no vaccine

Each year, the United States experiences an epidemic of the influenza virus. The epidemic usually starts in the late fall and is over by early spring. The influenza epidemic is caused primarily by influenza A and to a lesser extent by influenza B. The population remains susceptible to influenza because the viruses, especially influenza A, undergo frequent antigenic drift. The change in antigens is caused by point mutations and recombination events during viral replication.

Influenza is spread from individual to individual through close contact with respiratory droplets and less frequently by means of contaminated surfaces. The primary clinical manifestation of influenza is an acute respiratory illness. Influenza is differentiated from a common cold by the abrupt onset of systemic symptoms, such as fever, headache, myalgia, and weakness. The systemic symptoms usually are accompanied by signs, such as nonproductive cough, sore throat, and nasal congestion. The physical examination is usually unimpressive and typically the pulmonary examination is normal. Flushing from fever, mild cervical lymphadenopathy, and throat erythema may be the only physical findings.

Influenza is acutely debilitating but is usually self-limiting, lasting only 2–5 days. Complications from influenza can and do occur in high-risk populations. In fact, influenza is estimated to cause more than 36,000 deaths and more than 200,000 hospitalizations each year in the United States. The most common complication of influenza and indication for hospital admission is pneumonia. Pneumonia may be caused from the virus itself, a secondary bacterial infection, or a mixture of both. Other complications, such as myocarditis, pericarditis, meningitis, myositis, and Guillain-Barré syndrome can occur.

Patients at high risk of influenza complications are children younger than age 5 years, adults older than 65 years, and individuals with underlying medical complications (eg, asthma, diabetes mellitus, sickle cell disease, or immunosuppression). Although pregnant women are usually healthy, the physiologic and immunologic changes associated with pregnancy place a woman who is pregnant at increased risk of complications. A pregnant woman is 18 times more likely to require hospitalization with influenza compared with a healthy nonpregnant woman. For this reason, all pregnant women should be encouraged to receive the influenza vaccine.

The most effective prevention for influenza is immunization, and two types of vaccines are available:

1. Live attenuated influenza virus vaccine, administered as a nasal spray, is recommended for healthy people aged 2–49 years. The safety and effectiveness of the live attenuated influenza virus vaccination has not been studied in other populations and is not recommended during pregnancy.
2. Trivalent inactivated virus vaccine, administered by injection, should be given to high-risk individuals, such as pregnant women, and is considered safe to the fetus regardless of the gestational age at which the vaccine is administered.

The described patient should receive the injectable trivalent inactivated virus vaccine today. The numbers of stillbirths, congenital malformations, and malignancies are not increased in the offspring of pregnant women who receive the vaccine. Neurocognitive function is not affected by the vaccine either. Some multidose vials of the trivalent inactivated virus influenza vaccine contain thimerosal, a mercury-containing compound. The Institute of Medicine has reviewed the cumulative pediatric exposure to thimerosal-containing vaccines and has determined that no causal link exists between vaccinations and autism.

Mak TK, Mangtani P, Leese J, Watson JM, Pfeifer D. Influenza vaccination in pregnancy: current evidence and selected national policies. Lancet Infect Dis 2008;8:44–52.

Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2011. Centers for Disease Control and Prevention. MMWR Morb Mortal Wkly Rep 2011;60:1128–32.

Rothberg MB, Haessler SD, Brown RB. Complications of viral influenza. Am J Med 2008;121:258–64.

Tamma PD, Ault KA, del Rio C, Steinhoff MC, Halsey NA, Omer SB. Safety of influenza vaccination during pregnancy. Am J Obstet Gynecol 2009;201:547–52.

58

Genetic screening in women of Ashkenazi Jewish descent

A woman of Eastern European Ashkenazi Jewish descent is planning pregnancy. In addition to carrier screening for Tay–Sachs disease, Canavan disease, and cystic fibrosis, the American College of Obstetricians and Gynecologists (the College) recommends offering her carrier screening for

(A) Gaucher disease
(B) Bloom syndrome
(C) mucolipidosis IV
* (D) familial dysautonomia
(E) Fanconi anemia group C

Individuals of Eastern European Ashkenazi Jewish descent are at increased risk of genetic diseases that carry substantial morbidity and mortality. The large majority of the world's Jewish population resides in the United States and Israel. Among the Jewish population in the United States, most individuals are of Eastern European Ashkenazi descent. Tay–Sachs disease was one of the first genetic disorders for which screening programs were offered. The American College of Obstetricians and Gynecologists has recommended offering carrier screening for Tay–Sachs disease, cystic fibrosis, and Canavan disease. Recently, the College has added familial dysautonomia to the list of disorders for which carrier screening should be offered.

Familial dysautonomia is an autosomal recessive disorder. Two genes for familial dysautonomia were recently identified in patients of Ashkenazi Jewish descent. One of the mutations is found in more than 98% of patients with familial dysautonomia. It occurs almost exclusively in the Ashkenazi Jewish population with a carrier rate of 1 in 32. This rate is similar to that of Tay–Sachs disease and cystic fibrosis (Table 58-1). The clinical signs and symptoms of familial dysautonomia include abnormal suck and feeding difficulties, episodic vomiting, abnormal sweating, pain and temperature insensitivity, labile blood pressure, absent tearing, and scoliosis. There is no cure; however, treatment can improve length and quality of life. Life expectancy is diminished with up to 50% of affected individuals dying by age 30 years.

A family history and genetic history should be part of a preconception visit and a first prenatal visit. In general, people with this cultural background self identify as being of Ashkenazi Jewish descent when asked. At times, there may be uncertainty. It is considered appropriate to offer screening if the couple has one grandparent of Ashkenazi Jewish ancestry. Carrier screening should ideally occur before pregnancy. Preconception screening gives individuals time for partner screening if necessary and time to consider all potential diagnostic and reproductive options. Appropriate reproductive decisions also can be considered outside the context of an ongoing pregnancy.

Advances in genetics and technology have expanded the available options for genetic carrier detection. Individuals of Ashkenazi Jewish descent may ask about screening for other disorders for which carrier testing is available, such as Gaucher disease, Bloom syndrome, mucolipidosis IV, and Fanconi anemia group C (Table 58-1). Gaucher disease has a higher carrier frequency than other disorders that the College recommends offering carrier screening, however, there is variable expressivity of the disease (including asymptomatic affected individuals) and the availability of enzyme replacement therapy. Individuals should be given information about these disorders so that they can make an informed decision. At this time, the College does not recommend offering routine carrier screening for these disorders, and the American College of Medical Genetics does recommend routine screening in all Ashkenazi Jews.

TABLE 58-1. Recessive Genetic Diseases Frequent Among Individuals of Eastern European Jewish Descent Amenable to Carrier Screening

Disorder	Disease Incidence	Carrier Frequency*	Detection Rate*
Tay–Sachs disease	1/3,000	1/30	98% by hexosaminidase A test, 94% by DNA-based test
Canavan disease	1/6,400	1/40	98%
Cystic fibrosis	1/2,500–3,000	1/29	97%
Familial dysautonomia	1/3,600	1/32	99%
Fanconi anemia group C	1/32,000	1/89	99%
Niemann–Pick disease type A	1/32,000	1/90	95%
Mucolipidosis IV	1/62,500	1/127	95%
Bloom syndrome	1/40,000	1/100	95–97%
Gaucher disease	1/900	1/15	95%

* Non-Jewish carrier frequency and detection rates are unknown except for Tay–Sachs disease and cystic fibrosis. Carrier frequency for Tay–Sachs disease is 1 in 30 if French Canadian or Cajun ancestry and 1 in 300 for others with a 98% carrier detection rate by hexosaminidase A test.

Modified from March of Dimes. Genetic screening pocket facts. White Plains (NY): March of Dimes; 2001.

Preconception and prenatal carrier screening for genetic diseases in individuals of Eastern European Jewish descent. ACOG Committee Opinion No. 442. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:950–3.

Considerations when making decisions about carrier screening include prevalence of the disease, the carrier risk, disease severity and treatment options, cost, and reproductive choices. Patients may be assisted by a professional with expertise in genetic counseling in making an informed decision.

Gross SJ, Pletcher BA, Monaghan KG. Carrier screening in individuals of Ashkenazi Jewish descent. Professional Practice and Guidelines Committee. Genet Med 2008;10:54–6.

Klugman S, Gross SJ. Ashkenazi Jewish screening in the twenty-first century. Obstet Gynecol Clin North Am 2010;37:37–46.

Preconception and prenatal carrier screening for genetic diseases in individuals of Eastern European Jewish descent. ACOG Committee Opinion No. 442. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:950–3.

59

Complications of gastric bypass surgery in the obese parturient

A 37-year-old woman, gravida 2, para 1, comes to your office at 30 weeks of gestation with crampy abdominal pain and postprandial diarrhea. Before her pregnancy, she underwent Roux-en-Y gastric bypass surgery and lost 38.6 kg (85 lb). Her prepregnant body mass index (calculated as weight in kilograms divided by height in meters squared [kg/m^2]) (BMI) was 32.4. The pregnancy has been uncomplicated, and all of her obstetric laboratory values have been within normal limits. She is afebrile and her abdominal examination is unremarkable. The most likely source of her symptoms is

(A) bowel obstruction
(B) severe nutritional deficits
(C) anastomotic leak
* (D) dumping syndrome

Obesity creates a significant set of concerns with regard to prenatal risks and complications. With the epidemic of obesity in Western culture and the increasingly common deferral of childbearing to later years, it is common to encounter patients who are contemplating pregnancy after bariatric surgery. If the surgery has helped the patient to successfully lose weight, evidence suggests that her overall morbidity and mortality risks during pregnancy are less than those of an obese peer. However, the weight reduction strategy does carry some risks of its own. These risks include significant nutritional deficits as well as surgical complications, such as bowel obstruction, internal and ventral hernias, anastomotic leaks, and band erosion or migration.

Bowel obstruction was found in one study to be more common in bariatric patients than in a control cohort and, therefore, bowel obstruction should still be considered in the differential diagnosis for this patient's symptoms. Even though her symptoms are milder than would be expected with a partial or complete obstruction, obstetricians should be cautious about discarding this possibility, because obstruction may present somewhat atypically in pregnant women. Nonetheless, it is not the most likely diagnosis in the described patient.

Severe nutritional deficits are extremely likely in bariatric surgery patients who have not been monitored closely. Common deficiencies include protein, iron, vitamin B_{12}, folate, vitamin D, and calcium. Surveillance and prophylactic supplementation should be routine, and it is not appropriate to restrict protein or caloric intake, even if the patient remains obese. These deficits are usually of very gradual onset and may present with a variety of symptoms, but usually do not encompass gastrointestinal symptoms.

Anastomotic leaks are much less common now than in the past, primarily because of changes in bariatric surgery technique. Nonetheless, they can occur after any surgery in which an anastomosis was performed. Anastomotic leaks also may occur at a time very removed from the surgery. Thus, it is important to explore with the patient the type of surgery performed, and to acquire operative reports if possible. Anastomotic leaks generally are characterized by upper abdominal pain which is sharp, penetrating, and intense. If the obstetrician is unsure whether this complication is present, early consultation with a surgeon is appropriate, preferably with the surgeon who performed the bariatric procedure. However, this patient's more indolent presentation would argue against a diagnosis of anastomotic leak.

Dumping syndrome occurs when high glucose loads are delivered rapidly to the intestine, causing large osmotic fluid shifts into the lumen. This in turn creates distention, bloating, nausea, vomiting, and diarrhea. For this reason, caution should be exercised when administering concentrated glucose loads, such as in screening for gestational diabetes mellitus. Bariatric patients are given very strict restrictions postoperatively on both quality and quantity of food intake in order to avoid dumping syndrome. This patient fits the description of a patient with dumping syndrome given her postprandial diarrhea and benign abdominal examination.

Bariatric surgery and pregnancy. ACOG Practice Bulletin No. 105. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;113:1405–13.

Guelinckx I, Devlieger R, Vansant G. Reproductive outcome after bariatric surgery: a critical review. Hum Reprod Update 2009;15:189–201.

60

Periviable birth

A 30-year-old woman, gravida 3, para 2, comes to labor and delivery 7-cm dilated in active labor at 22 0/7 weeks of gestation. After discussion with the neonatologist regarding the lengthy hospital course, number of invasive procedures, and likely poor quality of life if the neonate survived, the parents request comfort care only for their premature newborn. The ethical principle that best guides the parents' decision making is

(A) beneficence
* (B) nonmaleficence
(C) justice
(D) autonomy

In counseling families with high risk of delivering a periviable neonate, information on death and disability rates should be given specific to the gestational age, estimated weight, and gender of the fetus. National data bank information, local intensive care nursery data, and consultation with a neonatologist can all be useful for estimating neonatal morbidity and mortality.

In general, mortality rates are inversely proportional to gestational age. Accurate assessment of gestational age and, if possible, transport to a tertiary care center can be helpful in guiding management. With current data, it is uncertain whether mode of delivery of the extremely premature infant affects survival. Use of corticosteroids in the periviable fetus is being investigated but administration is recommended at and beyond 24 weeks of gestation. Neonatal resuscitation efforts should be individualized depending on the status of the newborn, however, prediction of eventual outcome is challenging.

A medical ethics framework can assist patients and health care providers in making difficult medical decisions. Appropriate care of a premature infant at the cusp of viability is a difficult medical situation where standard medical care is likely to be ineffective. Health care providers are most familiar with a "principle-based" medical ethics framework. Other ethical frameworks might apply a different focus, such as case-based reasoning using prior precedent (such as legal decision making) or communitarian ethics, which adopts goals that are best for a community.

In a principle-based health care ethics system, four principles are used to identify and analyze ethical issues in a medical dilemma:

1. Autonomy
2. Beneficence
3. Nonmaleficence
4. Justice

Applying the principles can identify the conflicting obligations that make decision making challenging in these situations. Although the principles can be prioritized in a particular situation, there is considerable overlap in their application.

Autonomy suggests the right of individuals to make their own decisions. An example would be the right of an individual to decide whether to have surgery performed, and the expectation that adequate information will be given to inform that decision. The signing of an operative informed consent document reflects that autonomous decision. Actualizing autonomy assumes the patient has the mental capacity to engage in such a process, and that the patient's decision can be made with independence. Autonomy respects the moral right to bodily integrity and self-determination. Respect for the dignity of the individual and respect for the individual's worth are components of autonomy. Courts have upheld a woman's autonomy in making decisions that affect the outcome of the fetus. In the case of small children who lack the capacity to make informed decisions, under most circumstances parents are given the right to be surrogate decision makers.

As described in this case, to allow the parents to make the decision regarding the neonatal management plan after informing them of medical options is an example of the principle of autonomy. However, autonomy is not the guiding principle in the decision making. When performing a medical procedure is inevitably futile, it need not be offered. Respecting autonomy means that information is provided and a real decision requested. Thus, the parents did act with autonomy in this case, but the decision to palliate instead of treat was effectively made because of the obvious futility of treatment. There is a lack of effective interventions to promote benefit for the neonate and the more likely outcome of intervening will be increased suffering. As a result, the parents made a decision based on one of the other core principles.

Beneficence refers to actions that promote the well-being of others. Under the principle of beneficence, health care providers are required to act in the best interest of the patient. Although this might suggest that the neonatologist is obligated to resuscitate the periviable infant because no intervention is likely to result in death, beneficence is balanced with the principle of nonmaleficence.

Nonmaleficence suggests that medicine should "first, do no harm." The concept suggests that the potential for benefit of interventions should outweigh the possibility of needless harm. In the described scenario, in counseling the family, the neonatologist outlined the risks of intervention for the neonate. In this situation, the family saw the risks of intervention as being too great and likely futile and opted for comfort care. Although the principle of autonomy allowed them to make the decision, nonmaleficence guided the decision making process.

Justice concerns the fair distribution of resources and rendering to others what is due to them. The physician decides how to allocate limited resources and is obligated to treat equally those who are similar by some clinical criteria. Local and greater society also plays a role in justice. Community standards might dictate at which gestational age full resuscitation efforts should be extended to a periviable infant.

In many medical decisions in obstetrics, physicians have limited ability to predict the outcome. Applying an ethical framework or consulting someone experienced in the process may assist in decision making.

Batton B, Burnett C, Verhulst S, Batton D. Extremely preterm infant mortality rates and cesarean deliveries in the United States. Obstet Gynecol 2011;118:43–8.

Ethical decision making in obstetrics and gynecology. ACOG Committee Opinion No. 390. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;110:1479–87.

Fanaroff AA, Stoll BJ, Wright LL, Carlo WA, Ehrenkranz RA, Stark AR, et al. Trends in neonatal morbidity and mortality for very low birthweight infants. NICHD Neonatal Research Network. Am J Obstet Gynecol 2007;196:147.e1–8.

Fellman V, Hellström-Westas L, Norman M, Westgren M, Källén K, Lagercrantz H, et al. One-year survival of extremely preterm infants after active perinatal care in Sweden. EXPRESS Group. JAMA 2009;301:2225–33.

Hintz SR, Kendrick DE, Wilson-Costello DE, Das A, Bell EF, Vohr BR, et al. Early-childhood neurodevelopmental outcomes are not improving for infants born at <25 weeks' gestational age. NICHD Neonatal Research Network. Pediatrics 2011;127:62–70.

National Institutes of Health, Eunice Kennedy Shriver National Institute of Child Health & Human Development. NICHD Neonatal Research Network (NRN): extremely preterm birth outcome data. Rockville (MD): NIH; 2010. Available at: http://www.nichd.nih.gov/about/org/cdbpm/pp/prog_epbo/index.cfm. Retrieved June 11, 2012.

Perinatal care at the threshold of viability. ACOG Practice Bulletin No. 38. American College of Obstetricians and Gynecologists. Obstet Gynecol 2002;100:617–24.

Tomlinson MW, Kaempf JW, Ferguson LA, Stewart VT. Caring for the pregnant woman presenting at periviable gestation: acknowledging the ambiguity and uncertainty. Am J Obstet Gynecol 2010;202:529.e1–6.

Tyson JE, Parikh NA, Langer J, Green C, Higgins RD. Intensive care for extreme prematurity—moving beyond gestational age. National Institute of Child Health and Human Development Neonatal Research Network. N Engl J Med 2008;358:1672–81.

61
Asthma medications

A 19-year-old primigravid woman with asthma comes to you for a routine prenatal visit in the second trimester. She requests a refill of her prescription for albuterol. You inquire further and find that she has been using her albuterol metered dose inhaler up to 4 times a day for the past 2 weeks; this will be her third albuterol refill in a month. The most appropriate next step is to

(A) substitute a long-acting β_2-agonist
(B) refill her albuterol prescription alone
(C) alter the albuterol delivery method to nebulizer
* (D) add an inhaled corticosteroid
(E) add theophylline

Asthma is a common disease that affects up to 8% of pregnant women. This disease is more than simply bronchoconstriction. Rather, it is a disease of chronic airway inflammation, with increased airway responsiveness to many inciting stimuli. Thus, treatment, in all but the mildest intermittent cases, should be directed toward relieving airway inflammation.

The American College of Obstetricians and Gynecologists and the National Institutes of Health state that, "it is safer for pregnant women with asthma to be treated with medications than it is for them to have asthma symptoms and exacerbations." In addition to the use of medications, asthma management should include avoidance of or control of triggers, objective assessment of pulmonary function (spirometry or peak expiratory flow meter), and patient education.

Asthma may be mild intermittent, mild persistent, moderate persistent, or severe persistent, according to symptoms and pulmonary function testing (Table 61-1). Exacerbation during pregnancy is more likely in women with more severe degrees of asthma, but may occur even with mild disease. The described patient may have mild intermittent asthma and be experiencing an exacerbation, or may have inadequately controlled asthma of a more significant degree. To just prescribe more albuterol would be ineffective and may be dangerous. One of the risk factors for potentially fatal asthma is the use of more than two canisters of inhaled short-acting β_2-agonists per month.

Patient symptoms (including cough, wheezing, and subjective discomfort), amount of medication used, and objective measures of lung function must all be incorporated into the assessment. If optimal control is not demonstrated, the physician should assess technique of inhaler use, presence of environmental triggers (eg, smoking, pets, and indoor or outdoor air quality), and other factors that contribute to deterioration. There is no advantage in nebulized β_2-agonist treatments over a properly used metered dose inhaler. In most cases, a step up to the next level of pharmacologic control will be indicated. The dose, frequency, and number of medications should be increased as necessary, and decreased when feasible.

TABLE 61-1. Classification of Asthma Severity

Asthma Severity	Degree of Control	Symptom Frequency	Nighttime Awakening	Interference With Normal Activity	PEFR (% of Predicted or Best)
Mild intermittent	Well controlled	2 days per week or less	Twice a month or less	None	Greater than 80%
Mild persistent	Not well controlled	Greater than 2 days per week but less than daily	More than twice a month	Minor	Greater than 80%
Moderate persistent	Not well controlled	Daily	More than once a week	Some	60–80%
Severe persistent	Poorly controlled	Throughout the day	Greater than 4 times a week	Extreme	Greater than 60%

Abbreviation: PEFR, peak expiratory flow rate.

National Heart, Lung and Blood Institute and National Asthma Education and Prevention Program, Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full report 2007. Bethesda, MD: U.S. Department of Health and Human Services; p. 74.

Mild intermittent asthma usually can be managed adequately with a short-acting β_2-agonist, such as albuterol. However, a patient who requires a short-acting β_2-agonist more than twice in a week must be advanced to the next step, which will be the addition of a daily long-term controller medication. The preferred treatment is a daily inhaled corticosteroid, starting at a low dose. Although alternatives for mild persistent asthma include cromolyn, a leukotriene receptor antagonist, or theophylline, none of these is as effective as inhaled corticosteroids.

For moderate or severe asthma, steps three and four involve a long-acting β_2-agonist plus either a low-dose or medium-dose inhaled corticosteroid or the addition of systemic corticosteroids. At this stage, consultation with an asthma specialist is indicated. In the case of worsening symptoms, the physician should escalate treatment by two steps to gain control faster, and then step down therapy as the patient's condition improves. Figure 61-1 shows a stepwise approach for the management of asthma.

Pregnancy is not an indication for interrupting or altering asthma treatment. It appears that pregnant women are less likely to get recommended care than their nonpregnant counterparts and, therefore, are at more risk of continuing exacerbation. In a classic study of pregnant women who presented to emergency departments with asthma, fewer than 50% were given corticosteroids in the emergency department, and these women were only half as likely as nonpregnant patients to be prescribed

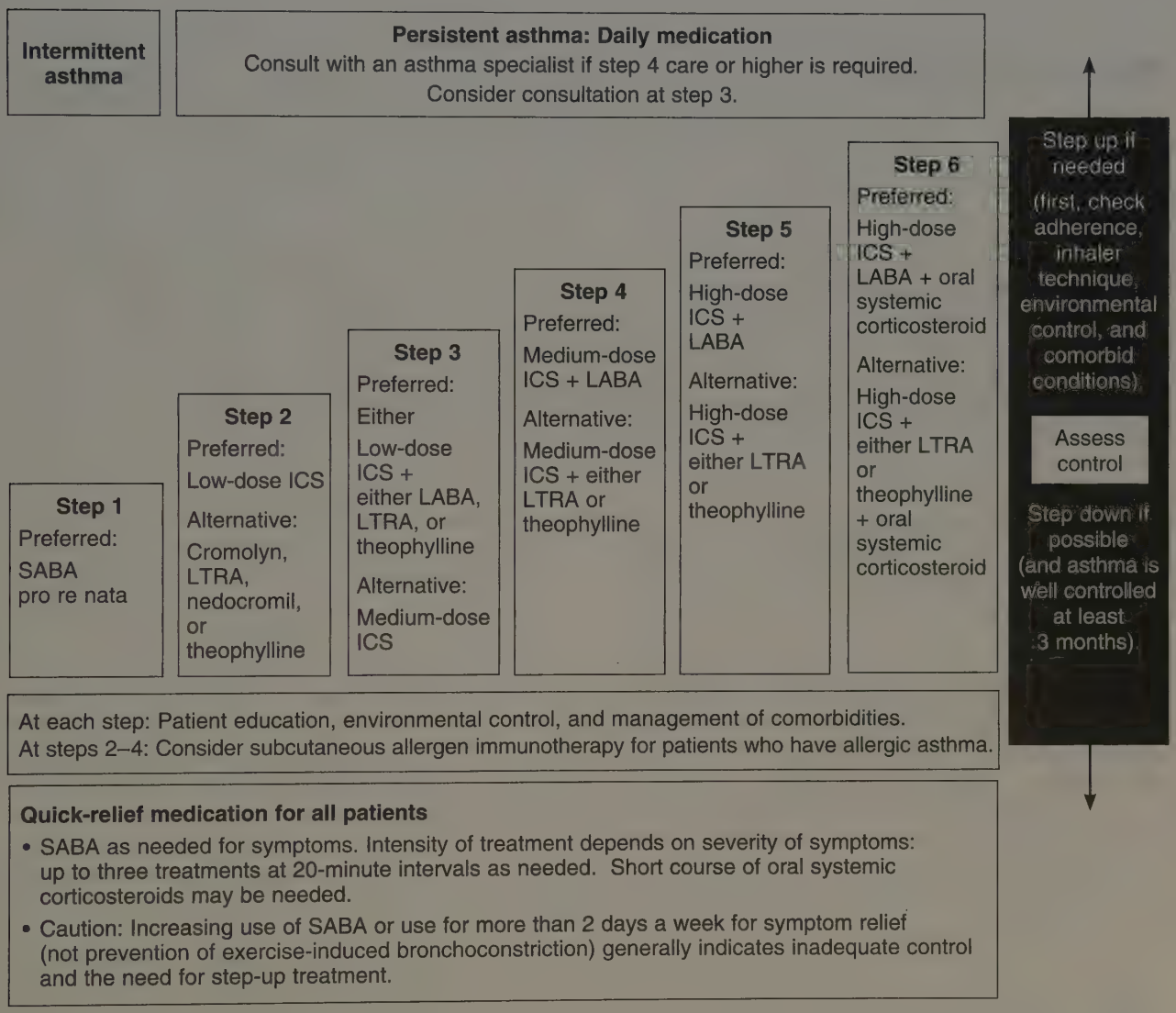

Intermittent asthma
Persistent asthma: Daily medication
Consult with an asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.
Step 1
Preferred:
SABA pro re nata
Step 2
Preferred:
Low-dose ICS
Alternative:
Cromolyn, LTRA, nedocromil, or theophylline
Step 3
Preferred:
Either
Low-dose ICS + either LABA, LTRA, or theophylline
Alternative:
Medium-dose ICS
Step 4
Preferred:
Medium-dose ICS + LABA
Alternative:
Medium-dose ICS + either LTRA or theophylline
Step 5
Preferred:
High-dose ICS + LABA
Alternative:
High-dose ICS + either LTRA or theophylline
Step 6
Preferred:
High-dose ICS + LABA + oral systemic corticosteroid
Alternative:
High-dose ICS + either LTRA or theophylline + oral systemic corticosteroid
Step up if needed
(first, check adherence, inhaler technique, environmental control, and comorbid conditions)
Assess control
Step down if possible (and asthma is well controlled at least 3 months)
At each step: Patient education, environmental control, and management of comorbidities.
At steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma.
Quick-relief medication for all patients
• SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to three treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
• Caution: Increasing use of SABA or use for more than 2 days a week for symptom relief (not prevention of exercise-induced bronchoconstriction) generally indicates inadequate control and the need for step-up treatment.

FIG. 61-1. Stepwise approach for the management of asthma. Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. Abbreviations: ICS, inhaled corticosteroid; LABA, inhaled long-acting β_2-agonist; LTRA, leukotriene receptor agonist; SABA, inhaled short-acting β_2-agonist. (Modified from Expert Panel Report 3: guidelines for the diagnosis and management of asthma. National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program. Bethesda (MD): National Institutes of Health; 2007. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Retrieved October 7, 2011; June 11, 2012.)

corticosteroids for outpatient use, a factor which may explain the nearly threefold increase in ongoing exacerbations at 2-week follow-up.

Guidelines on home and hospital management of asthma in pregnancy are available at http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg/astpreg_qr.pdf. Included are sample action plans which can be customized for the individual patient.

Asthma in pregnancy. ACOG Practice Bulletin No. 90. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008; 111:457–64.

Cydulka RK. Acute asthma during pregnancy. Immunol Allergy Clin North Am 2006;26:103–17.

Cydulka RK, Emerman CL, Schreiber D, Molander KH, Woodruff PG, Camargo CA Jr. Acute asthma among pregnant women presenting to the emergency department. Am J Respir Crit Care Med 1999;160:887–92.

Expert Panel Report 3: guidelines for the diagnosis and management of asthma. National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program. Bethesda (MD): National Institutes of Health; 2007. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Retrieved June 11, 2012.

Restrepo RD, Peters J. Near-fatal asthma: recognition and management. Curr Opin Pulm Med 2008;14:13–23.

Schatz M, Dombrowski MP. Clinical practice. Asthma in pregnancy. N Engl J Med 2009;360:1862–9.

Working Group report on managing asthma during pregnancy; recommendations for pharmacologic treatment: update 2004. National Heart, Lung, and Blood Institute, National Asthma Education Program, Working Group on Asthma and Pregnancy. Bethesda (MD): National Heart, Lung, and Blood Institute; 2005. Available at: http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg/astpreg_full.pdf. Retrieved September 14, 2009; June 11, 2012.

62

Intrauterine growth restriction

A 33-year-old woman, gravida 3, para 2, at 32 6/7 weeks of gestation is referred for ultrasonography for fetal growth because of a fundal height measuring 28 cm. First-trimester risk assessment demonstrated low risks for Down syndrome and trisomy 18. She has had chronic hypertension for 5 years, controlled with labetalol hydrochloride twice daily during this pregnancy. Her blood pressure today is 134/82 mm Hg. Ultrasonography demonstrates a fetus with an estimated fetal weight in the 7th percentile. Amniotic fluid index is 8.2 cm and the biophysical profile is 8/8. The best umbilical artery Doppler parameter to aid assessment for delivery is

(A) peak systolic velocity
* (B) end diastolic flow
(C) pulsatility index
(D) systolic/diastolic (S/D) ratio

Intrauterine growth restriction (IUGR), defined as an estimated fetal weight less than the 10th percentile for gestational age, is associated with increased risk of perinatal mortality and neurologic morbidity. This definition poorly distinguishes between normal and pathologic growth, and may include a substantial number of fetuses that are constitutionally small. Adverse perinatal outcomes largely are confined to infants with birth weights less than the fifth percentile.

Within the ultrasonographic biometric indices, abdominal circumference is the most specific indicator for IUGR associated with uteroplacental pathology. Evaluation of fetal blood flow with the use of Doppler ultrasonography can improve the specificity and is an important evaluation and surveillance tool in IUGR. Increased resistance in the placenta, a common cause of IUGR, impairs diastolic blood flow and can be detected with Doppler velocimetry. Use of umbilical artery Doppler ultrasonography for IUGR has been associated with a reduction in perinatal mortality, along with lower rates of induction and cesarean delivery.

As placental resistance increases, diastolic flow through the umbilical artery is impaired. This initially may cause an increase in the S/D ratio and eventually can lead to absent or reversed diastolic flow, indicating further worsening of placental status, and thus, fetal status. Although the S/D ratio is an important parameter for umbilical artery Doppler ultrasonography in cases of fetal growth restriction, the most important characteristic is the presence or absence of diastolic flow, because absent and reversed diastolic flow are signs of severe compromise. These should be considered concerning findings and

may even provoke a decision for delivery. Peak systolic velocity and pulsatility index are less useful parameters in evaluation and surveillance of growth restriction.

Not all fetuses with pathologic growth restriction will exhibit abnormal findings on umbilical artery Doppler ultrasonography. Other fetal vessels, such as the middle cerebral artery and the ductus venosus, allow for detection of the fetal response to adverse intrauterine conditions in the antepartum period.

Alfirevic Z, Stampalija T, Gyte GML. Fetal and umbilical Doppler ultrasound in high-risk pregnancies. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD007529. DOI: 10.1002/14651858.CD007529.pub2.

American College of Obstetricians and Gynecologists. Intrauterine growth restriction. ACOG Practice Bulletin 12. Washington, DC: ACOG; 2000.

McIntire DD, Bloom SL, Casey BM, Leveno KJ. Birth weight in relation to morbidity and mortality among newborn infants. N Engl J Med 1999;340:1234–8.

63

Air travel

A 38-year-old woman, gravida 3, para 1, at 24 weeks of gestation comes to your clinic for a routine prenatal visit. She reports a planned overseas business trip next week. Her obstetric history identifies two previous spontaneous preterm deliveries at 28 weeks and 27 weeks of gestation. Her current pregnancy is complicated by asthma, which is controlled with intermittent albuterol use. You advise her that she should avoid air travel primarily because of concerns related to

(A) hypoxia
* (B) preterm delivery
(C) radiation exposure
(D) thrombosis

Multiple theoretical concerns have been expressed regarding air travel in pregnancy. However, relatively few studies, especially prospective studies, are available to guide health care providers and their patients. The environment of an aircraft cabin offers hazards that are infrequently encountered in other settings, including exposure to ionizing radiation, lower oxygen partial pressures, prolonged hypomobility, increased noise, infectious hazards, very low humidity, and limited access to medical care. Although it is preferable to minimize these risks during pregnancy, the actual effect of infrequent travel by air is poorly understood.

In the United States, residents are exposed to approximately 6 milliSieverts of radiation annually from all sources (cosmic radiation, medical procedures, and radon). Cosmic radiation exposure is increased with increasing altitude and time aloft. Commercial flights may reach cruising altitudes of 12,192 m (40,000 ft), which reduce the protective effect of the atmosphere. The recommended radiation exposure limit in pregnancy is 1 milliSievert. Typical radiation exposure during flight is 0.04 microSieverts per minute of flight time. Intercontinental flights may reach up to 15% of the 1-milliSievert limit. Infrequent air travel should therefore be safe. If patients are members of air crews on regular long-haul flights, they may need to alter their work plans for pregnancy.

The added radiation exposure from airport security scanners using backscatter X-ray technology is 0.03–0.1 (mcSv) per scan. This exposure represents a negligible increase in risk, equivalent to another 1–3 minutes of flying time. Patients also may be reassured to learn that it would require 200,000 airport scans to reach the radiation exposure of an abdominal computed tomography scan, a study that may be used in pregnancy when medically indicated, and which does not exceed the recommended radiation exposure limit for pregnancy.

Increased risk of thrombosis should be considered for all pregnant patients. Decreased mobility and dehydration from a low-humidity environment can exacerbate the stasis and hypercoagulable state of every pregnancy. A meta-analysis of 10 randomized trials that examined the effect of wearing compression stockings on flights longer than 7 hours found a substantial decrease (odds ratio [OR] = 0.10, 95% confidence interval [CI] 0.04–0.25, $P<.001$) in asymptomatic deep vein thrombosis. There were no symptomatic deep vein thrombosis or pulmonary emboli in the trials. Whether the protection would accrue to pregnant patients is uncertain, but the possible benefits of wearing compression stockings for long flights would exceed any yet to be defined risks.

Commercial aircraft cabins usually are pressurized to altitudes of 2,438 m (8,000 ft). Increases in blood

pressure and heart rate and a decrease in aerobic capacity have been found to be associated with this pressure altitude, but the effect of these changes on pregnancy is not known. The same lack of prospective data for guidance is true regarding noise levels, infectious exposures, and vibration. Seat belt use will protect patients from potential trauma related to unpredicted turbulence. Seat belts should be worn low across the hips, under the gravid abdomen, and if a shoulder belt is available, it should be worn across the clavicle and between the breasts.

A meta-analysis examined the effect of air travel and found an increased risk of preterm birth less than 37 weeks of gestation (OR = 1.44, 95% CI 1.07–1.93), but no increased risk of preeclampsia, admissions to intensive care nurseries, or birth weight less than the 10th percentile for gestational age. The same meta-analysis found that flight attendants have higher rates of spontaneous abortion or intrauterine fetal demise than controls (OR = 1.62, 95% CI 1.29–2.04).

In the described patient, all of the reasons for possible concern are valid, but her risk of preterm delivery, indicated by her obstetric history, is the biggest worry. This patient should be advised to avoid travel for the duration of her pregnancy because of her risk of preterm birth. If there is a true effect on preterm birth as suggested by the aforementioned described meta-analysis, the recommendation would be even more valid.

More specific recommendations may need to be considered for patients who fly frequently, participate in flight activities with the military, work as pilots, or otherwise have more exposure to risks associated with flight. For infrequent travelers without medical or obstetric contraindications to flight, the advice is the same as for nonpregnant travelers: the riskiest part of the journey is the drive to the airport.

Air travel during pregnancy. ACOG Committee Opinion No. 443. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:954–5.

Chibber R, Al-Sibai MH, Qahtani N. Adverse outcome of pregnancy following air travel: a myth or a concern? Aust N Z J Obstet Gynaecol 2006;46:24–8.

Clarke MJ, Hopewell S, Juszczak E, Eisinga A, Kjeldstrøm M. Compression stockings for preventing deep vein thrombosis in airline passengers. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD004002. DOI: 10.1002/14651858.CD004002.pub2.

Freeman M, Ghidini A, Spong CY, Tchabo N, Bannon PZ, Pezzullo JC. Does air travel affect pregnancy outcome? Arch Gynecol Obstet 2004;269:274–7.

Magann EF, Chauhan SP, Dahlke JD, McKelvey SS, Watson EM, Morrison JC. Air travel and pregnancy outcomes: a review of pregnancy regulations and outcomes for passengers, flight attendants, and aviators. Obstet Gynecol Surv 2010;65:396–402.

Mehta P, Smith-Bindman R. Airport full-body screening: what is the risk? Arch Intern Med 2011;171:1112–5.

64

Epidural complications

A 24-year-old primigravid woman at 39 weeks of gestation comes to the hospital in active labor. She requests epidural analgesia. Aside from hypotension, the most likely complication to be associated with her epidural anesthesia is

(A) cesarean delivery
(B) chronic back pain
(C) fetal heart rate decelerations
* (D) fever
(E) postdural puncture headache

Epidural anesthesia is a safe, effective means of providing pain control to patients who are in labor. It should be provided for pain relief at maternal request, and is the most common form of regional obstetric anesthesia used in the United States. Serious complications related to regional anesthesia are extremely rare. The case-fatality rate for regional anesthesia during cesarean delivery is estimated at 1.9 per 1,000,000 live births.

Concerns expressed in regard to increased cesarean delivery rates in patients who use epidural anesthesia were based on studies published before 2000. In the past decade, randomized trials and meta-analyses that have examined the effect of epidural anesthesia on the risk of cesarean delivery have shown that epidural anesthesia does not affect cesarean delivery rates, and recommendations were changed accordingly. Current recommendations also support the administration of epidural anesthesia at any time in labor rather than waiting until the active phase is reached.

Complications related to regional anesthesia are listed in Table 64-1. Rare but serious complications related to epidural use include complete spinal blockade, epidural or spinal hematoma, abscess, neurotoxicity, and meningitis. Less serious but very bothersome to the patient is postdural puncture headache. Blood patch treatment may be needed in more than 36% of cases of postdural puncture headache after epidural placement because the unintentional dural puncture usually is created with a larger needle.

Common complications of epidural anesthesia include pruritus, fever, hypotension, transient fetal heart rate decelerations, and inadequate pain relief. Pruritus that occurs after epidural opioids are used can be treated with naloxone or nalbuphine. Hypotension can be modulated but not prevented by preanesthetic hydration. Pretreatment with ephedrine is not effective for prevention of hypotension, but ephedrine may be needed to avoid altered uterine perfusion in hypotensive patients. Transient fetal heart rate decelerations may occur with epidural use but typically respond to conservative management, including hydration, oxygenation, position changes, and ephedrine administration.

The occurrence of fever in patients with epidurals is a poorly understood phenomenon. It does not appear to be related to infectious causes. Inflammation may play a role as demonstrated by the finding that women with high interleukin-6 levels were at increased risk of fever after epidural placement. A randomized trial of acetaminophen versus placebo in the prevention of epidural fever found the same rate of fever in each group, suggesting that the temperature response may not be mediated centrally. Fever related to epidural increases neonatal sepsis evaluations, neonatal antibiotic administration, and the risk of maternal antibiotic administration. However, there is no increase in cases of neonatal sepsis. In nulliparous patients, fever is one of the most common complications of epidural use.

Some retrospective studies suggest a link between epidural use and chronic back pain. Methodologic problems, such as recall bias, make interpretation of these findings difficult. In prospective cohort studies and in one randomized trial, however, no association was identified between epidural use and chronic back pain.

Analgesia and cesarean delivery rates. ACOG Committee Opinion No. 339. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006;107:1487–8.

Goetzl L, Rivers J, Evans T, Citron DR, Richardson BE, Lieberman E, et al. Prophylactic acetaminophen does not prevent epidural fever in nulliparous women: a double-blind placebo-controlled trial. J Perinatol 2004;24:471–5.

Obstetric analgesia and anesthesia. ACOG Practice Bulletin No. 36. American College of Obstetricians and Gynecologists. Obstet Gynecol 2002;100:177–91.

Riley LE, Celi AC, Onderdonk AB, Roberts DJ, Johnson LC, Tsen LC, et al. Association of epidural–related fever and noninfectious inflammation in term labor. Obstet Gynecol 2011;117:588–95.

Sharma SK, Alexander JM, Messick G, Bloom SL, McIntire DD, Wiley J, et al. Cesarean delivery: a randomized trial of epidural analgesia versus intravenous meperidine analgesia during labor in nulliparous women. Anesthesiology 2002;96:546–51.

TABLE 64-1. Complications of Regional Analgesia

Complication	Incidence (%)
Hypotension (in prehydrated women undergoing cesarean delivery)	
Spinal	25–67[1,2]
Epidural (in prehydrated women in labor)	28–31[3–5]
Epidural	8.5–9[6,7]
Fever >38°C (>100.4°F) (excess rate over women treated with narcotics)	
Nulliparous women	19[8]
Multiparous women	1[8]
Postdural puncture headache	
Spinal	1.5–3[9,10]
Epidural	2[11]
Combined spinal epidural	1–2.77[11–13]
Transient fetal heart decelerations	8[14]
Pruritus (with added opioid only)	
Epidural	1.3–26[11,15]
Spinal and combined spinal epidural	41–85[16,17,11,18]
Inadequate pain relief: epidural	9–15[19,6]

[1]Vercauteren MP, Coppejans HC, Hoffmann VH, Mertens E, Adriaensen HA. Prevention of hypotension by a single 5-mg dose of ephedrine during small-dose spinal anesthesia in prehydrated cesarean delivery patients. Anesth Analg 2000;90:324–7.

[2]Park GE, Hauch MA, Curlin F, Datta S, Bader AM. The effects of varying volumes of crystalloid administration before cesarean delivery on maternal hemodynamics and colloid osmotic pressure. Anesth Analg 1996;83:299–303.

[3]Fong J, Gurewitsch ED, Press RA, Gomillion MC, Volpe L. Prevention of maternal hypotension by epidural administration of ephedrine sulfate during lumbar epidural anesthesia for cesarean section. Am J Obstet Gynecol 1996;175:985–90.

[4]Sharma SK, Sidawi JE, Ramin SM, Lucas MJ, Leveno KJ, Cunningham FG. Cesarean delivery: a randomized trial of epidural versus patient-controlled meperidine analgesia during labor. Anesthesiology 1997;87:487–94.

[5]Brizgys RV, Dailey PA, Shnider SM, Kotelko DM, Levinson G. The incidence and neonatal effects of maternal hypotension during epidural anesthesia for cesarean section. Anesthesiology 1987;67:782–6.

[6]Eberle RL, Norris MC, Eberle AM, Naulty JS, Arkoosh VA. The effect of maternal position on fetal heart rate during epidural or intrathecal labor analgesia. Am J Obstet Gynecol 1998;179:150–5.

[7]Collis RE, Davies DW, Aveling W. Randomized comparison of combined spinal-epidural and standard epidural analgesia in labour. Lancet 1995;345:1413–6.

[8]Philip J, Alexander JM, Sharma SK, Leveno KJ, McIntire DD, Wiley J. Epidural analgesia during labor and maternal fever. Anesthesiology 1999;90:1271–5.

[9]Sears DH, Leeman MI, Jassy LJ, O'Donnell LA, Allen SG, Reisner LS. The frequency of postdural puncture headache in obstetric patients: a prospective study comparing the 24-gauge versus the 22-gauge Sprotte needle. J Clin Anesth 1994;6:42–6.

[10]Vallejo MC, Mandell GL, Sabo DP, Ramanathan S. Postdural puncture headache: a randomized comparison of five spinal needles in obstetric patients. Anesth Analg 2000;91:916–20.

[11]Norris MC, Grieco WM, Borkowski M, Leighton BL, Arkoosh VA, Huffnagle HJ, et al. Complications of labor analgesia: epidural versus combined spinal epidural techniques. Anesth Analg 1994;79:529–37.

[12]Collis RE, Plaat FS, Morgan BM. Comparison of midwife top-ups, continuous infusion and patient-controlled epidural analgesia for maintaining mobility after a lowdose combined spinal-epidural. Br J Anaesth 1999;82:233–6.

[13]Herbstman CH, Jaffee JB, Tuman KJ, Newman LM. An in vivo evaluation of four spinal needles used for the combined spinal-epidural technique. Anesth Analg 1998;86:520–2.

[14]Palmer CM, Maciulla JE, Cork RC, Nogami WM, Gossler K, Alves D. The incidence of fetal heart rate changes after intrathecal fentanyl labor analgesia. Anesth Analg 1999;88:577–81.

[15]Vertommen JD, Vandermeulen E, Van Aken H, Vaes L, Soetens M, Van Steenberge A, et al. The effects of the addition of sufentanil to 0.125% bupivacaine on the quality of analgesia during labor and on the incidence of instrumental deliveries. Anesthesiology 1991;74:809–14.

[16]Gambling DR, Sharma SK, Ramin SM, Lucas MJ, Leveno KJ, Wiley J, et al. A randomized study of combined spinal-epidural analgesia versus intravenous meperidine during labor: impact on cesarean delivery rate. Anesthesiology 1998;89:1336–44.

[17]Dahl JB, Jeppesen IS, Jorgensen H, Wetterslev J, Moiniche S. Intraoperative and postoperative analgesic efficacy and adverse effects of intrathecal opioids in patients undergoing cesarean section with spinal anesthesia: a qualitative and quantitative systematic review of randomized controlled trials. Anesthesiology 1999;91:1919–27.

[18]Shah MK, Sia AT, Chong JL. The effect of the addition of ropivacaine or bupivacaine upon pruritus induced by intrathecal fentanyl in labour. Anaesthesia 2000;55:1008–13.

[19]Beilin Y, Zahn J, Bernstein HH, Zucker-Pinchoff B, Zenzen WJ, Andres LA. Treatment of incomplete analgesia after placement of an epidural catheter and administration of local anesthetic for women in labor. Anesthesiology 1998;88:1502–6.

65

Shoulder dystocia

During the birth of her first child, a patient experienced a shoulder dystocia relieved by McRoberts maneuver and delivery of the posterior arm. In the patient's next pregnancy, she would like to have another vaginal delivery. You counsel her that the recurrence risk of shoulder dystocia is approximately

(A) 1–5%
* (B) 10–15%
(C) 25–35%
(D) greater than 50%

Shoulder dystocia is an uncommon and unpredictable obstetric emergency. Shoulder dystocia is diagnosed when normal downward traction on the fetal head fails to complete a vaginal delivery and additional obstetric maneuvers are needed. The most common obstetric maneuver used is the McRoberts maneuver, ie, hyperflexion and abduction of the hips. If necessary, suprapubic pressure may be used at the same time to help dislodge the impacted shoulder. Fetal manipulation with either a rotational maneuver or delivery of the posterior arm also can be used. In catastrophic cases where the shoulder dystocia is not relieved by repeated attempts with these maneuvers, cephalic replacement with cesarean delivery may be used.

A number of risk factors for shoulder dystocia have been identified. Fetal macrosomia and maternal diabetes mellitus are the most commonly reported risk factors. Other antenatal factors include maternal obesity, multiparity, postdates pregnancy, prior macrosomic newborn, and previous history of a delivery complicated by shoulder dystocia. Intrapartum factors include labor induction, epidural anesthesia, and operative vaginal delivery. No single risk factor or combination of risk factors can predict shoulder dystocia with enough accuracy to be useful clinically. Clinical strategies, such as induction of labor to prevent macrosomia and shoulder dystocia, have increased the risk of cesarean delivery without decreasing the risk of shoulder dystocia. Approximately one half of all deliveries complicated by shoulder dystocia occur in women who have no risk factors.

Overall, the recurrence risk of shoulder dystocia in a subsequent pregnancy is approximately 10–15%. Because the recurrence risk in subsequent pregnancies is relatively low, the patient may opt for a vaginal delivery or a cesarean delivery after counseling. Presence of certain clinical factors may aid the health care provider in counseling the patient, such as the severity of the prior shoulder dystocia, current estimated fetal weight compared with the birth weight of the prior infant, and the presence of diabetes mellitus.

If a shoulder dystocia occurs, the fetus is at risk of injury. Injuries that may be associated with shoulder dystocia include fractured clavicle, fractured humerus, or a brachial plexus injury. A fractured clavicle or humerus usually heals without any residual damage. The reported range of brachial plexus injury after a vaginal birth complicated by a shoulder dystocia varies widely from 4% to 40%. Most cases resolve and only approximately 10% of infants have permanent neurologic injury. Rarely, in severe cases of shoulder dystocia the fetus may suffer hypoxic–ischemic encephalopathy or death.

Bingham J, Chauhan SP, Hayes E, Gherman R, Lewis D. Recurrent shoulder dystocia: a review. Obstet Gynecol Surv 2010;65:183–8.

Doumouchtsis SK, Arulkumaran S. Is it possible to reduce obstetrical brachial plexus palsy by optimal management of shoulder dystocia? Ann N Y Acad Sci 2010;1205:135–43.

Gherman RB. Shoulder dystocia: an evidence-based evaluation of the obstetric nightmare. Clin Obstet Gynecol 2002;45:345–62.

Shoulder dystocia. ACOG Practice Bulletin No. 40. American College of Obstetricians and Gynecologists. Obstet Gynecol 2002;100:1045–50.

66
Mastitis

A 27-year-old woman, 2 weeks postpartum, comes to your office with fever and pain in the left breast. She has been exclusively breastfeeding since giving birth. She has no known drug allergies. Her temperature is 39°C (102°F). You observe a wedge-shaped area of redness and tenderness on the upper outer quadrant of the left breast and no discrete mass is palpated. The right breast is unremarkable. After 2 days of antibiotic therapy with dicloxacillin and no improvement, a breast milk culture reveals methicillin-resistant *Staphylococcus aureus* (MRSA). The best next step in pharmacotherapy is to prescribe

(A) cefazolin
(B) cephalexin
(C) erythromycin
(D) amoxicillin–clavulanate
* (E) trimethoprim–sulfamethoxazole

Breastfeeding is important for the promotion of both infant and maternal health. Approximately 75% of women in the United States initiate breastfeeding. The Healthy People 2020 Goal calls for an increase of breastfeeding to 82%. Because breastfeeding is so common, the obstetrician–gynecologist must be familiar with how to treat its complications. Lactational mastitis occurs in approximately 2–10% of lactating women and is the most common inflammatory breast disorder. It usually occurs during the second to fourth week postpartum.

The diagnosis of lactational mastitis is made clinically. Symptoms include unilateral breast pain and a tender, wedge-shaped area of redness extending from the nipple. Fever, malaise, and myalgia are frequently present. Milk culture should be strongly considered, especially in cases where there is no prompt resolution of symptoms. The predominant organisms responsible for mastitis are *S aureus* in approximately 50% of cases. Less frequently, the causative organism can be group A or group B *streptococci, Escherichia coli,* or anaerobic *Bacteroides* species. Methicillin-resistant *S aureus* is another emerging community-acquired pathogen that is known to cause mastitis.

Treatment of mastitis consists of relief of symptoms with analgesics, such as acetaminophen or ibuprofen; antibiotics; and continued emptying of the breast by breastfeeding and pumping. Breastfeeding from the affected breast does not pose a problem for a healthy infant.

The preferred first-line antibiotic agents for the treatment of uncomplicated mastitis are penicillinase-resistant penicillins, such as dicloxacillin. First generation cephalosporins also are acceptable but are less preferred because of their broader spectrum. For patients who are allergic to penicillin, clindamycin or erythromycin may be used.

When a culture is positive or the history is suggestive of exposure or colonization with MRSA, standard therapy should be used. In addition, in women who fail to respond to standard therapy, MRSA should be considered. Antibiotics that maintain activity against most community-acquired MRSA include trimethoprim–sulfamethoxazole, tetracycline, clindamycin, vancomycin, and rifampin. Of these, trimethoprim–sulfamethoxazole is a commonly used oral agent for outpatient management. However, MRSA is resistant to β-lactam antibiotics, including penicillinase-resistant penicillin (dicloxacillin); penicillins combined with a β-lactamase inhibitor (amoxicillin–clavulanate); and cephalosporins (cefazolin, cephalexin).

Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. The puerperium. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams obstetrics. 23rd ed. New York (NY): McGraw-Hill Medical Publishing Division; 2010. p. 646–60.

Pearlman MD, Griffin JL. Benign breast disease. Obstet Gynecol 2010; 116:747–58.

67

Pulmonary embolism

A 29-year-old primigravid woman presents with unilateral leg edema and dyspnea at 24 weeks of gestation. A pulmonary embolus is diagnosed by means of computed tomography angiography. At admission, she had a platelet count of 289,000/mm^3. Unfractionated intravenous heparin was begun; 3 days later, she reports generalized easy bruisability and is found to have a platelet count of 40,000/mm^3. In addition to stopping heparin, the best next step in her management is

(A) change to warfarin
(B) placement of a vena caval filter
* (C) change to fondaparinux sodium
(D) administer protamine sulfate

Heparin-induced thrombocytopenia is a feared and serious complication of heparin therapy. It is an absolute contraindication to further exposure to heparin, including low molecular weight heparin, because it provokes a prothrombotic state that can lead to devastating thromboembolic events.

Initiation of warfarin has substantial fetal consequences because it may cross the placenta and cause intracranial hemorrhage in the third trimester. Protamine sulfate reverses the action of heparin on the coagulation factors and would not improve platelet function.

Fondaparinux sodium is a relatively new therapy that works via anti-Xa and anti-IXa activity and is the best next step in management for the described patient. Fondaparinux does not cross the placenta and, thus, is unlikely to cause fetal harm. It has been used in pregnancy and has not been associated with teratogenicity or fetal bleeding. Unlike argatroban, it can be given subcutaneously as an outpatient. Because of its unique mechanism of action, it does not affect platelet physiology.

After the initiation of heparin therapy, most clinical guidelines advocate checking platelet count 5–10 days after the first dose. This strategy will discover many, but not all, instances of this complication. It can appear later in the treatment course and health care providers should have a low threshold for doing platelet counts with any symptom of platelet dysfunction.

Heparin-induced thrombocytopenia is a rare but serious harm of anticoagulation. Other more common adverse effects include skin rashes, bruising, gastrointestinal bleeding, and bone loss. Although radiographic loss of bone is common, fractures are very rare. Patients on heparin should be encouraged to report any gastrointestinal bleeding, melena, and bruising other than at the injection site.

Patients who take anticoagulants should take precautions to avoid situations that can provoke trauma. Contact sports, working on ladders, or rigorous leisure activities can provoke bleeding and hematoma formation. Health care providers who prescribe anticoagulants should take careful occupational and social histories to learn about any risky behaviors and advise against them.

Bates SM, Greer IA, Hirsh J, Ginsberg JS. Use of antithrombotic agents during pregnancy: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004;126:627S–44S.

Donovan JL, Tran MT, Kanaan AO. An overview of heparin-induced thrombocytopenia. J Pharm Pract 2010;23:226–34.

Ekbatani A, Asaro LR, Malinow AM. Anticoagulation with argatroban in a parturient with heparin-induced thrombocytopenia. Int J Obstet Anesth 2010;19:82–7.

Lassila R, Antovic JP, Armstrong E, Baghaei F, Dalsgaard-Nielsen J, Hillarp A, et al. Practical viewpoints on the diagnosis and management of heparin–induced thrombocytopenia. Semin Thromb Hemost 2011;37:328–36.

Ortel TL. Heparin-induced thrombocytopenia: when a low platelet count is a mandate for anticoagulation. Hematology Am Soc Hematol Educ Program 2009;225–32.

Thromboembolism in pregnancy. Practice Bulletin No. 123. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:718–29.

Walfisch A, Koren G. The "warfarin window" in pregnancy: the importance of half–life. J Obstet Gynaecol Can 2010;32:988–9.

68

Vanity or keepsake ultrasonography

During a review with your office staff of next year's business plan you solicit ideas for adding new sources of revenue. You are considering beginning an off-site facility that offers fetal keepsake three-dimensional ultrasonographic scans and videos. After reviewing statements from the American College of Obstetricians and Gynecologists, the U.S. Food and Drug Administration, and the American Institute of Ultrasound in Medicine, you note that they

* (A) discourage this activity because of the nonmedical use of diagnostic equipment
(B) have no opinion on this commercial enterprise
(C) support such activities only if proper supervision can be assured
(D) require the same level of record documentation as in an office setting

Ultrasonography for entertainment purposes—also known as "keepsake" or "vanity" ultrasonography—has become increasingly popular. Some medical facilities have attempted to accommodate patients who wish to have an entertaining experience, and entrepreneurial marketing and easy accessibility have made this type of ultrasonography an appealing option. However, its use should not be advocated.

Adverse fetal effects of prenatal ultrasonography have not been demonstrated. However, ultrasonography uses a form of energy that at higher exposure levels, such as in lithotripsy or deep tissue therapy, can produce heat and tissue destruction. Ultrasonography carried out in unregulated and unsupervised facilities does not ensure that energy (eg, mechanical and thermal index ratings) and exposure levels are maintained appropriately.

The U.S. Food and Drug Administration views ultrasonography for entertainment purposes as an unapproved use of a medical device that provides no medical benefit. At this time, however, enforcement has been left to local agencies. Individuals or agencies that use diagnostic equipment without the order of a licensed professional may be in violation of state or local laws or regulations regarding use of a prescription medical device. Furthermore, this may constitute practice of medicine without a license.

The American Institute of Ultrasound in Medicine has issued a statement on "Prudent Use in Obstetrics," which states that it "advocates the responsible use of diagnostic ultrasound and strongly discourages the non-medical use of ultrasound for entertainment purposes. The use of ultrasound without a medical indication to view the fetus, obtain a picture of the fetus or determine the fetal gender is inappropriate and contrary to responsible medical practice. Ultrasound should be used by qualified health professionals to provide medical benefit to the patient."

The American College of Obstetricians and Gynecologists agrees with the position of the American Institute of Ultrasound in Medicine to discourage the use of ultrasonography for nonmedical purposes and cautions that ultrasonography may provide false reassurance. Despite disclaimers about the limitations of keepsake ultrasonography, women and their families may take it as proof of a healthy fetus or, conversely, an incidental finding may provoke anxiety.

Although a medical office may not offer an ultrasonographic experience at the level of a dedicated ultrasonography facility, to offer the patient photographs and an enjoyable experience within a medical context can satisfy most patients' desires.

American Institute of Ultrasound in Medicine. Entertainment ultrasound [patient page]. Laurel (MD): AIUM; 2012. Available at: http://www.aium.org/patients/entertainment.aspx. Retrieved June 11, 2012.

American Institute of Ultrasound in Medicine. Keepsake fetal imaging. Laurel (MD): AIUM; 2012. Available at: http://www.aium.org/publications/viewStatement.aspx?id=31. Retrieved June 11, 2012.

Food and Drug Administration. Avoid fetal "keepsake" images, heartbeat monitors. Silver Spring (MD): FDA; 2008. Available at: http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/ucm095602.pdf. Retrieved June 11, 2012.

Greene N, Platt LD. Nonmedical use of ultrasound: greater harm than good? J Ultrasound Med 2005;24:123–5.

Houston LE, Odibo AO, Macones GA. The safety of obstetrical ultrasound: a review. Prenat Diagn 2009;29:1204–12.

Nonmedical use of obstetric ultrasonography. ACOG Committee Opinion No. 297. American College of Obstetricians and Gynecologists. Obstet Gynecol 2004;104:423–4.

Rados C. FDA cautions against ultrasounds 'keepsake' images. FDA Consum 2004;38:12–6.

69
Fetal death

A 30-year-old woman, gravida 5, para 4, comes to the hospital at 35 weeks of gestation with decreased fetal movement. Her prior pregnancies were uncomplicated and she has no medical problems. Midtrimester anatomy ultrasonography showed choroid plexus cyst and fetal heart defect. She declined genetic testing and her prenatal laboratory results were otherwise normal. Fetal monitoring and ultrasonography reveal absent fetal heart beat, and a diagnosis of fetal demise is made. Her vital signs are normal including a blood pressure reading of 110/70 mm Hg. The test(s) most likely to be informative regarding the cause of the stillbirth is (are)

(A) maternal protein S and protein C levels
(B) hemoglobin A_{1C}
* (C) amniocentesis for karyotype
(D) complete blood count with platelets and urinalysis for protein and liver enzymes
(E) titers for toxoplasmosis, other viruses, rubella, cytomegalovirus, herpes simplex viruses

Proper evaluation of stillbirth leads to an identifiable cause in approximately one half of cases (Box 69-1 and Fig. 69-1). Identification of the cause of stillbirth is extremely important to patients as they mourn their loss and look for an explanation. The risk of recurrence is increased twofold to 10-fold and is partially based on the underlying etiology. Identification of a cause will allow, where appropriate, prevention, and treatment in future pregnancies in order to decrease the risk of recurrence.

An abnormal karyotype is found in approximately 8–13% of stillbirths. If there are structural abnormalities or growth restriction, the rate exceeds 20%. The most common abnormalities are monosomy X (23%), trisomy 21 (23%), trisomy 18 (21%), and trisomy 13 (8%). In the described case with choroid plexus cyst and fetal heart defect, the probability of fetal aneuploidy is increased. Fetal karyotypic evaluation after delivery is often noninformative because of delay in time from death to delivery and tissue autolysis.

Acceptable cytologic specimens for karyotype include amniotic fluid obtained by amniocentesis, placental block taken from below the cord insertion site, umbilical cord

BOX 69-1

Status of Evaluation for Stillbirth

Generally accepted tests
- Fetal autopsy
- Placental evaluation
- Karyotype
- Indirect Coombs test
- Serologic test for syphilis
- Screen for fetal–maternal hemorrhage (Kleihauer-Betke test or other)
- Toxicology screen
- Thorough medical and obstetric history
- Parvovirus serology

Useful in some cases
- Lupus anticoagulant screen
- Anticardiolipin antibodies
- Factor V Leiden mutation
- Prothrombin *G20210A* mutation
- Screen for protein C, protein S, and antithrombin III deficiency

Uncertain utility
- Thyroid-stimulating hormone
- Glycohemoglobin
- Toxoplasmosis, rubella, cytomegalovirus, and herpes simplex (TORCH) titers
- Placental cultures
- Testing for other thrombophilias

Developing technology
- Comparative genomic hybridization
- Testing for single-gene mutations
- Testing for confined placental mosaicism
- Nucleic acid-based testing for infection

Reprinted from Silver RM, Varner MW, Reddy U, Goldenberg R, Pinar H, Conway D, et al. Work-up of stillbirth: a review of the evidence. Am J Obstet Gynecol 2007;196:433–44.

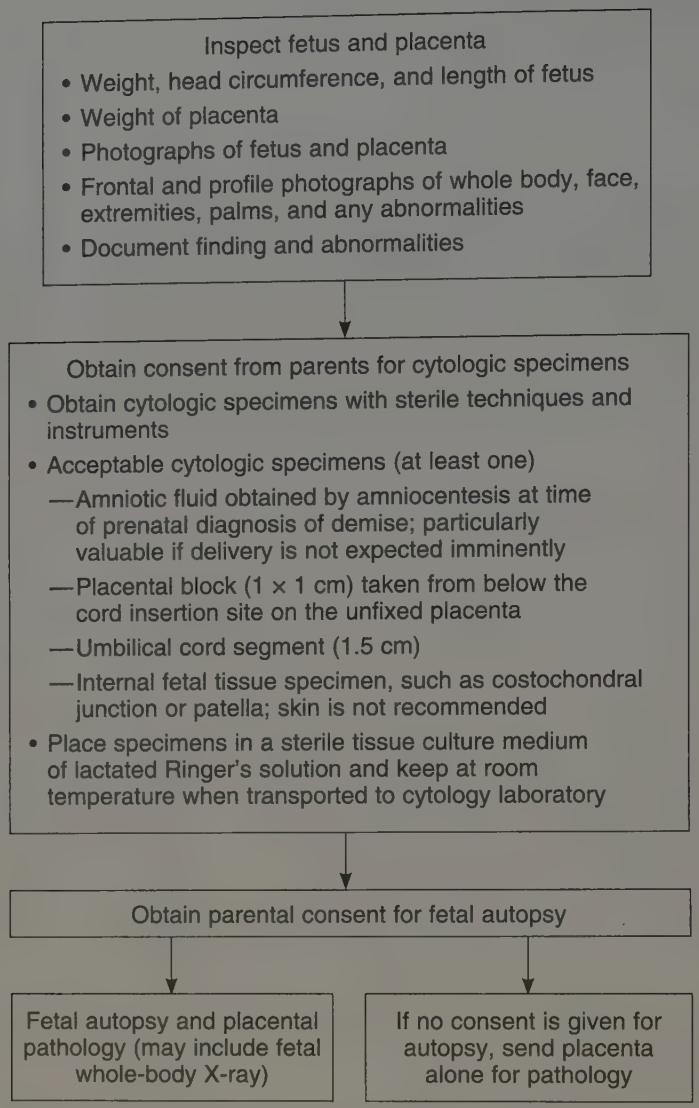

Inspect fetus and placenta
• Weight, head circumference, and length of fetus
• Weight of placenta
• Photographs of fetus and placenta
• Frontal and profile photographs of whole body, face, extremities, palms, and any abnormalities
• Document finding and abnormalities
Obtain consent from parents for cytologic specimens
• Obtain cytologic specimens with sterile techniques and instruments
• Acceptable cytologic specimens (at least one)
—Amniotic fluid obtained by amniocentesis at time of prenatal diagnosis of demise; particularly valuable if delivery is not expected imminently
—Placental block (1 × 1 cm) taken from below the cord insertion site on the unfixed placenta
—Umbilical cord segment (1.5 cm)
—Internal fetal tissue specimen, such as costochondral junction or patella; skin is not recommended
• Place specimens in a sterile tissue culture medium of lactated Ringer's solution and keep at room temperature when transported to cytology laboratory
Obtain parental consent for fetal autopsy
Fetal autopsy and placental pathology (may include fetal whole-body X-ray)
If no consent is given for autopsy, send placenta alone for pathology

FIG. 69-1. Flowchart for fetal and placental evaluation. (Management of stillbirth. ACOG Practice Bulletin No. 102. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;113:748–61.)

segment, and fetal tissue segment, such as costochondral junction or patella. Of these options, a sample of cells obtained by amniocentesis represents the technique most likely to produce cell growth to give karyotype.

An autopsy is one of the most important tests for determination of the cause of stillbirth. Careful evaluation of fetal anatomic structures and placental histopathology can prove informative. It is often a challenge to convince grieving parents of the clinical utility and importance of the fetal autopsy, but it can have important clinical ramifications for management of future pregnancies.

Given the patient's normal laboratory results earlier in pregnancy and no prior history of diabetes mellitus, the likelihood of glucose intolerance as the cause of her stillbirth is low. Protein S and protein C levels are known to be unreliable because of the confounding effects of pregnancy. If it is clinically indicated that protein S and protein C levels should be measured, they should be assessed after 6 weeks postpartum. Laboratory testing for complete blood count, protein, and liver enzymes usually is done in combination with clinical evaluation for preeclampsia. In this case with normal blood pressure, no other signs of preeclampsia, and the presence of an abnormal fetal ultrasonography, preeclampsia is not likely to be a cause. The role of routine maternal antibody testing (eg, toxoplasmosis, other viruses, rubella, cytomegalovirus, herpes simplex virus titers) as a workup for congenital infection in stillbirth cases remains the subject of debate. In the described case, if an amniocentesis is being performed, amniotic fluid studies for viral culture and polymerase chain reaction test for parvovirus and cytomegalovirus may be better options.

Association between stillbirth and risk factors known at pregnancy confirmation. Stillbirth Collaborative Research Network Writing Group. JAMA 2011;306:2469–79.

Causes of death among stillbirths. Stillbirth Collaborative Research Network Writing Group. JAMA 2011;306:2459–68.

Haws RA, Yakoob MY, Soomro T, Menezes EV, Darmstadt GL, Bhutta ZA. Reducing stillbirths: screening and monitoring during pregnancy and labour. BMC Pregnancy Childbirth 2009;9 Suppl 1:S5.

Maternal–Fetal Medicine Committee, Clinical Practice Obstetrics Committee, Leduc L, Farine D, Armson BA, Brunner M, et al. Stillbirth and bereavement: guidelines for stillbirth investigation. J Obstet Gynaecol Can 2006;28:540–52.

Silver RM, Varner MW, Reddy U, Goldenberg R, Pinar H, Conway D, et al. Work-up of stillbirth: a review of the evidence. Am J Obstet Gynecol 2007;196:433–44.

70

Complications of anesthesia

An obese primigravid 18-year-old woman is admitted to the hospital nonresponsive after a seizure. She is at 36 weeks of gestation by bedside ultrasonography. Breathing is stertorous and pulse oximetry is 80% on room air. Blood pressure is 180/110 mm Hg. A portable chest X-ray result is negative. You administer magnesium sulfate and decide to perform a cesarean delivery because of eclampsia and because the fetus is in breech presentation. General anesthesia is induced and the trachea is intubated. During the procedure, the anesthesiologist reports difficulty maintaining oxygen saturation at greater than 85%. The most likely explanation is

(A) pulmonary edema
(B) acute respiratory distress syndrome (ARDS)
* (C) aspiration
(D) mainstem intubation
(E) anaphylaxis

In 1946, New York anesthesiologist, C. L. Mendelson published a case series of 66 deliveries under ether anesthesia, which were complicated by aspiration of gastric contents into the lungs. In less than 10% of cases, solid material presented as airway obstruction and aspiration of liquid contents produced cyanosis, dyspnea, tachycardia, and pulmonary edema. Dr. Mendelson was able to reproduce the same constellation of findings in rabbits when he instilled hydrochloric acid into their lungs. Chemical pneumonitis from aspiration of acidic gastric contents during obstetric anesthesia is now known as Mendelson syndrome.

The stomach produces approximately 1.5 L of fluid daily, with a pH as low as 1.0, containing not only acid but the proteolytic enzyme pepsin. If food particles, blood, or infectious material also are aspirated, further damage may occur. Normal surfactant is replaced by an exudate of fibrin, inflammatory cells, and hemorrhage, so lung compliance is reduced, lung volume is decreased, lung water is increased, and intrapulmonary shunting occurs. The net effect is pulmonary edema and hypoxemia, with cellular debris plugging smaller bronchioles. Release of inflammatory mediators produces the common signs and symptoms of acute lung injury or ARDS, ie, dyspnea, tachypnea, tachycardia, widened alveolar–arterial oxygen gradient or frank hypoxemia, wheezing, rales, and abnormal chest X-ray findings. Because the right mainstem bronchus is more nearly vertical than the left, aspiration is preferentially directed toward the right lower lobe. However, infiltrates may be seen bilaterally. Because radiographic findings often lag many hours behind the clinical event, the chest X-ray may be normal shortly after aspiration.

Presence of normal airway reflexes is generally sufficient to guard against aspiration, even in pregnancy when gastric volumes are increased and the lower esophageal sphincter is relaxed. Some individuals with altered states of consciousness are at risk of aspiration (ie, drug or alcohol effects, general anesthesia, head trauma, and seizures). Because most aspiration events are unwitnessed, aspiration pneumonitis may be mistaken for another entity, eg, bacterial pneumonia.

Additional risk factors for aspiration include pregnancy, obesity, diabetes mellitus, dysphagia, vomiting, and esophageal or gastrointestinal disorders. Although advanced age is a known risk factor, this would be irrelevant in obstetrics. Pulmonary edema may be a consequence of aspiration, but is not a risk factor; the same is true for ARDS.

Aspiration is difficult to diagnose unless witnessed. The recovery of food particles from the trachea, although convincing, is rare. Silent aspiration, aspiration before presenting for medical care, or aspiration of gastric liquid without food particles is much more common. Because there is no standard diagnostic test, aspiration is frequently a diagnosis of exclusion; thus, it is important to keep the index of suspicion high. A patient at increased risk of aspiration, who demonstrates hypoxemia or other signs consistent with aspiration, should be considered to have aspirated gastric contents even if the event has not been witnessed.

The development of respiratory failure should be treated in the standard manner, with supplemental oxygen, tracheal intubation, and mechanical ventilation. Another indication for intubation would be ongoing inability to protect her airway, such as intoxication, status epilepticus, or a postictal state. If respiratory compromise is suspected without respiratory failure, the patient may be nursed in a head-up position and given humidified oxygen and bronchodilators, while being closely monitored for deterioration. A nasogastric tube should be inserted and the stomach kept empty, all in an attempt to prevent another episode.

In most cases, bronchoscopy is not indicated. With aspiration of liquids, bronchoscopy only serves to disperse the material further. Antibiotics often are given, which may reflect an uncertainty about the diagnosis. Aspiration of acid material is not by itself an infectious process. Aspiration-induced lung injury is a risk factor for the development of bacterial pneumonia, with organisms akin to any other hospital-acquired or ventilator-associated pneumonia.

Because general anesthesia is known to increase the risk of aspiration, several management principles have been promulgated to lessen that risk. When possible, regional anesthesia is preferred to general anesthesia. If general anesthesia is being used in a pregnant patient, the anesthesiologist would prefer

- no food by mouth except for modest amounts of clear liquids, which may be given up to 2 hours before anesthesia.
- preanesthesia neutralization of acid stomach contents, using a nonparticulate antacid.
- rapid sequence induction of anesthesia with cricoid pressure to prevent regurgitation until the trachea is successfully intubated.
- avoidance of techniques that depress airway reflexes unless the airway is secured with a cuffed endotracheal tube.
- awake extubation.

H_2 blockers also may be given before anesthesia in order to decrease gastric acidity. This approach has proven successful in decreasing anesthesia-related maternal mortality and severe morbidity, but, unfortunately, cannot be expected to play a role in preventing aspiration outside of the operating room.

In the case described, her history alone should raise suspicion for aspiration: a pregnant woman with impaired airway reflexes who now demonstrates desaturation. This event seems to have occurred before her arrival at the hospital, as peripheral oxygen desaturation is seen on admission; thus, it is unlikely that a right mainstem endobronchial intubation accounts for this patient's degree of oxygen desaturation. However, endobronchial intubation is always a possibility when an endotracheal tube is inserted too far. Pulmonary edema would be evident on the chest X-ray. The diagnosis of ARDS requires both clinical and radiographic components which are not met in the patient described, viz, a ratio of partial pressure of oxygen in arterial blood to fraction of inspired oxygen (Pao_2/Fio_2) gradient less than 200 in the presence of bilateral infiltrates without evidence of left ventricular failure. Anaphylaxis may present with desaturation and wheezing, but would more likely be accompanied by hypotension.

Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, et al. Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006–2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. BJOG 2011;118 Suppl 1:1–203.

Hawkins JL, Chang J, Palmer SK, Gibbs CP, Callaghan WM. Anesthesia-related maternal mortality in the United States: 1979–2002. Obstet Gynecol 2011;117:69–74.

Mendelson CL. The aspiration of stomach contents into the lungs during obstetric anesthesia. Am J Obstet Gynecol 1946;52:191–205.

O'Sullivan G, Hari MS. Aspiration: risk, prophylaxis, and treatment. In: Chestnut DH, Polley LS, Tsen LC, Wong CA, editors. Chestnut's obstetric anesthesia: principles and practice. 4th ed. Philadelphia (PA): Mosby Elsevier; 2009. p. 633–50.

Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Anesthesiology 2007;106:843–63.

Raghavendran K, Nemzek J, Napolitano LM, Knight PR. Aspiration-induced lung injury. Crit Care Med 2011;39:818–26.

71

Legal and ethical obligations in patient transfer

You are covering your labor and delivery unit (level 1 nursery) when a patient arrives by ambulance. She reports that she is "7 months along" and has been experiencing abdominal pain for several days. She also thinks that she has had vaginal fluid leakage. Maternal vital signs are stable and there is no evidence of bleeding. Ultrasonography indicates a 28-week fetus, a transverse lie, and an amniotic fluid index of 2 cm. External monitoring shows contractions every 4–8 minutes, and a Category III fetal heart rate tracing. The fetal heart rate tracing does not improve with maternal oxygen supplementation, position change, or intravenous fluids. Her cervix is 1 cm dilated. The best next step in management is

(A) arrange transfer to a tertiary care center
(B) amniotransfusion
* (C) expeditious delivery at your facility
(D) tocolysis

The concept of regionalized health interventions has proven extremely effective in improving outcomes for compromised neonates. Low-risk deliveries may be managed at smaller, more remote facilities. Patients with risk factors, or those who develop problems, may be transported to facilities with more sophisticated intervention options and more specialized personnel.

For optimal results, both the transferring and accepting facilities must be completely clear about their responsibility for the patient's management. Therefore, Federal guidelines have been established under the Emergency Medical Treatment and Active Labor Act to define these elements of responsibility. Each obstetrician should be familiar with these guidelines, both for clinical use and to serve as a reference for hospital leadership and program developers.

The facility to which the patient initially presents must, under Emergency Medical Treatment and Active Labor Act regulations, assess the patient with "an appropriate medical screening examination." At some facilities, the screening examination will include, at a minimum, evaluation of maternal vital signs, assessment of the fetus (including electronic fetal monitoring if available and appropriate), assessment of the fetal position, and a maternal cervical examination if the patient is contracting and the examination is not otherwise contraindicated.

The original facility is responsible for a thorough assessment of the patient's condition and stability before initiation of transport. An unstable patient should be managed until stability for transport can be achieved, even if it requires delivering and then transporting either the mother, the infant, or both. In the described case, the Category III fetal heart rate tracing, which did not improve with interventions, necessitates expeditious delivery and would not allow transfer. The neonate can then be transferred as needed by the pediatric staff, after stabilization in the original facility.

Given the patient's instability, transfer to a tertiary care facility, either by ground or air, should not be arranged because such management delays delivery and risks morbidity and mortality for the baby. Neither amniotransfusion nor tocolysis is indicated given the Category III fetal heart rate tracing.

Some high-risk facilities have transport teams available to come to outlying facilities and accompany the patient to definitive care, whereas others accept transfers but offer no transport assistance. It is the responsibility of the referring health care provider to monitor and care for the patient until the accepting team physically receives the patient. This does not mean that the referring health care provider must always accompany the patient. If the patient is truly stable enough for transport, it is rarely necessary for the health care provider to accompany the patient in the transport. However, the transport team should be consistent with the expected level of medical need during the transport.

The burden of good judgment falls heavily on the referring facility and health care provider. This can be quite challenging if there is little obstetric experience from which to decide management. The receiving tertiary care center can be supportive in helping the sending facility to work through the decision steps, but must never encourage a transport that does not seem safe. Ultimately, it is the decision making of the sending health care provider that will be scrutinized.

If transfer of a stable patient occurs, there is a real and strong burden on the tertiary care facility to provide appropriate communication back regarding the patient's condition, and particularly on transport back to the original facility. All too often, a patient arrives "back home"

after an extended stay in a high-risk environment and those who will be providing ongoing care have insufficient information in regard to interventions performed and goals expected and achieved. It is clearly incumbent on the receiving facility to complete a thorough discharge plan including a summary of the patient's hospital course and anticipated future needs.

In complex cases where ongoing extended service will be required (such as home health visits or physical therapy), a predischarge contact is needed to ensure that such services are available at the original facility. Thorough and sensitive communication is the best means to bridge the gap between the tertiary care center and the low-risk medical environment.

American Academy of Pediatrics, American College of Obstetricians and Gynecologists. Guidelines for perinatal care. 7th ed. Elk Grove Village (IL): Washington, DC: AAP; ACOG; 2012.

Cardwell MS. Interhospital transfers of obstetric patients under the Emergency Medical Treatment and Active Labor Act. J Leg Med 1995;16:357–72.

Glass DL, Rebstock J, Handberg E. Emergency Treatment and Labor Act (EMTALA). Avoiding the pitfalls. J Perinat Neonatal Nurs 2004; 18:103,14; quiz 115–6.

72

Imitators of severe preeclampsia

A 36-year-old woman, gravida 1, para 0, at 32 weeks of gestation with known systemic lupus erythematosus (SLE) comes to your office for a routine prenatal visit. She has lupus nephritis with 2 g of protein in 24 hours. Her pregnancy has thus far proceeded normally although she has experienced mild arthritic symptoms with pain and discomfort in her joints. She has been taking no medication for her SLE other than nonsteroidal antiinflammatory drugs. She is now experiencing headache and increased pedal edema (+3). She is found to have hypertension (blood pressure 150/100 mm Hg) and her temperature is 38.1°C (100.6°F). Her laboratory results show a hemoglobin level 10.2 g/dL, platelet count 160,000/mm^3, glucose level 98 mg/dL, and an increased 24-hour urinary protein of 4 g. Her levels of ammonia, liver enzymes, lactate dehydrogenase, and bilirubin are all in the normal range. The most likely diagnosis is

(A) hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome
(B) thrombotic thrombocytopenia purpura (TTP)
(C) hemolytic uremic syndrome (HUS)
* (D) exacerbation of SLE
(E) acute fatty liver of pregnancy

Determination of the etiology of new onset symptoms of headache, hypertension, and edema in women with known SLE is often challenging. Because these women often have preexisting hypertension and proteinuria, other signs and symptoms are necessary to make an accurate diagnosis. The treatment for preeclampsia is delivery, and an SLE flare may be treated with anti-inflammatory medications and pregnancy continuation, depending on the patient's gestational age. This difference in treatment may have profound repercussions.

Central nervous system symptoms and fever are common symptoms of SLE flare, and increased proteinuria often is seen, especially in patients with SLE nephritis. Hepatic abnormalities, such as jaundice and laboratory results of increased levels on liver function tests, ammonia, and bilirubin, are very uncommon with SLE flares. Additionally, low glucose level and thrombocytopenia are also unusual and if present should point to another diagnosis. Although it may take several days for the laboratory results to be received, hypocomplementemia (C_3, C_4, C_{50}), if present, may help confirm the diagnosis. In some situations, a trial of immunosuppressive agents (eg, glucocorticoids, intravenous immunoglobulin) is recommended; if there is response then the diagnosis of flare is confirmed.

There are several other less common but serious conditions that are considered to be imitators of severe preeclampsia–eclampsia, including acute fatty liver of pregnancy, TTP, and HUS. Women with HELLP syndrome may have nausea, vomiting, and right abdominal pain. Laboratory abnormalities include increased liver enzymes (eg, bilirubin, transaminases, and lactate dehydrogenase), thrombocytopenia, and anemia. Acute fatty liver of pregnancy can have similar presentation, but usually has a progressive and prompt deterioration of

maternal condition. The presence of hypoglycemia and development of severe hepatic dysfunction, manifested as elevated ammonia levels, is highly suggestive of acute fatty liver of pregnancy; TTP–HUS may manifest with fever, CNS symptoms, nausea, and abdominal pain. Laboratory findings with these conditions often demonstrate evidence of anemia and hemolysis, which is uncommon with SLE flare. Tables 72-1 and 72-2, respectively, show frequency and severity of signs and symptoms and the frequency and severity of laboratory findings among imitators of preeclampsia–eclampsia.

Egerman RS, Ramsey RD, Kao LW, Bringman JJ, Bush AJ, Wan JY. Hypertensive disease in pregnancies complicated by systemic lupus erythematosus. Am J Obstet Gynecol 2005;193:1676–9.

Kamen B, Karwal MA, Yankowitz J. Hemolysis and elevated transaminases imitating severe preeclampsia. Obstet Gynecol 2009;113:545–7.

Sibai BM. Imitators of severe preeclampsia. Obstet Gynecol 2007;109: 956–66.

TABLE 72-1. Frequency of Various Signs and Symptoms Among Imitators of Preeclampsia–Eclampsia*

Signs and Symptoms	HELLP Syndrome	AFLP	TTP	HUS	Exacerbation of SLE
Hypertension	85	50	20–75	80–90	80 with APA, nephritis
Proteinuria	80–95	30–50	With hematuria	80–90	100 with nephritis
Fever	Absent	25–32	20–50	NR	Common during flare
Jaundice	5–10	40–90	Rare	Rare	Absent
Nausea and vomiting	40	50–80	Common	Common	Only with APA
Abdominal pain	60–80	35–50	Common	Common	Only with APA
Central nervous system	40–60	30–40	60–70	NR	50 with APA

* Data are %.

Abbreviations: AFLP, acute fatty liver of pregnancy; APA, antiphospholipid antibodies with or without catastrophic antiphospholipid syndrome; Common, reported as the most common presentation; HELLP syndrome, hemolysis, elevated liver enzymes, and low platelet count syndrome; HUS, hemolytic uremic syndrome; NR, values not reported; SLE, systemic lupus erythematosus; TTP, thrombotic thrombocytopenia purpura.

Sibai BM. Imitators of severe preeclampsia. Obstet Gynecol 2007;109:956–66.

TABLE 72-2. Frequency and Severity of Laboratory Findings Among Imitators of Preeclampsia–Eclampsia

Signs and Symptoms	HELLP Syndrome	AFLP	TTP	HUS	Exacerbation of SLE
Thrombocytopenia (less than 100,000/mm^3)	More than 20,000	More than 50,000	20,000 or less	More than 20,000	More than 20,000
Hemolysis (%)	50–100	15–20	100	100	14–23 with APA
Anemia (%)	Less than 50	Absent	100	100	14–23 with APA
DIC (%)	Less than 20	50–100	Rare	Rare	Rare
Hypoglycemia (%)	Absent	50–100	Absent	Absent	Absent
VW factor multimers (%)	Absent	Absent	80–90	80	Less than 10
ADAMTS13 less than 5% (%)	Absent	Absent	33–100	Rare	Rare
Impaired renal function (%)	50	90–100	30	100	40–80
LDH (IU/L)	600 or more	Variable	More than 1,000	More than 1,000	With APA
Elevated ammonia (%)	Rare	50	Absent	Absent	Absent
Elevated bilirubin (%)	50–60	100	100	N/A	Less than 10
Elevated transaminases (%)	100	100	Usually mild*	Usually mild*	With APA

*Levels less than 100 IU/L.

Abbreviations: ADAMTS13, von Willebrand factor-cleaving metalloprotease; AFLP, acute fatty liver of pregnancy; DIC, disseminated intravascular coagulation; APA, antiphospholipid antibodies; HELLP syndrome, hemolysis, elevated liver enzymes, and low platelet count syndrome; HUS, hemolytic uremic syndrome; LDH, lactic dehydrogenase; SLE, systemic lupus erythematosus; N/A, not available; TTP, thrombotic thrombocytopenia purpura.;

Sibai BM. Imitators of severe preeclampsia. Obstet Gynecol 2007;109:956–66.

73

Headache

A 26-year-old woman, gravida 1, at 18 weeks of gestation consults you because of headache. The pain is unilateral, throbbing in nature, and worsens with movement of her head, light, and sound. She has no nausea, visual changes, nasal congestion, or lacrimation. Her headache is episodic, occurs approximately 1–2 times per month, and is relieved by ibuprofen. The most likely type of headache is

(A) sinus
(B) cluster
(C) tension
* (D) migraine
(E) hemicrania continua

Headache is a common disorder that has a major effect on society. Up to 14% of women and 8% of men miss all or part of a day at work or school each month because of headache. It is a major cause of emergency room visits and accounts for approximately 1.1% of all office visits. Primary headache disorders are responsible for most headaches. Migraine headache is a common primary headache disorder affecting approximately 18% of women, and is the most likely diagnosis in this patient. The current view is that migraine is caused by a neurologic dysfunction and is not a vascular disorder. It involves a disorder of the subcortical aminergic sensory modulatory systems and likely includes the brainstem, and the hypothalamic and thalamic structures.

International Headache Society criteria for the diagnosis of migraine require a repeated episodic headache lasting 4–72 hours and any two of the following characteristics: unilateral, throbbing, worsened by movement, moderate or severe; and any one of: nausea–vomiting, photophobia, or phonophobia. No single feature is mandatory except that the headache must be recurrent. Classic migraine includes aura and is found in up to 30% of people who suffer from migraine.

Migraines often get worse in the first trimester of pregnancy, but many women will have a reduction in the frequency of migraine in the second and third trimesters. Approximately 25% of migraine patients will have no change in the severity or frequency of migraines in pregnancy. Women with menstrual migraines may improve in pregnancy. Given the described patient's symptoms, her most likely type of headache is migraine.

Other headache disorders have symptoms that overlap with those of migraine. Sinus headaches often are confused because of location. Sinus headache is often unilateral; however, it also is associated with signs and symptoms of rhinosinusitis, facial pain, congestion of the nose, and nasal discharge.

Cluster headaches are also unilateral. They are rare and occur in a series that lasts for weeks or months, and can occur from every other day to eight episodes per day. Cluster headaches are suborbital or temporal and are associated with autonomic symptoms, such as nasal congestion or lacrimation.

Tension headache is the most common, episodic headache. It has no aura; the pain is dull, and nonpulsatile with the sensation of tightness, pressure, or constriction. Most tension headaches are bilateral. Hemicrania continua is a very rare type of headache. It is continuous, waxing and waning, and moderate to severe in intensity. Like migraine it is unilateral, but it is not worsened by movement.

Secondary causes of headache, such as intracranial mass, subarachnoid hemorrhage, and subdural hematoma, are important to diagnose because of the potential for severe morbidity and mortality. Although not present in the described case, certain alarms raise the suspicion of a secondary cause, ie,

- onset after age 50 years.
- sudden onset.
- new onset with cancer or human immunodeficiency virus (HIV).
- systemic symptoms (fever, stiff neck, rash).
- focal neurologic signs and symptoms (other than typical aura).
- papilledema.

If a patient with recurrent headaches exhibits such characteristics, further investigation should be carried out by means of imaging or other testing.

Goadsby PJ. Pathophysiology of migraine. Neurol Clin 2009;27:335–60.

Lay CL, Broner SW. Migraine in women. Neurol Clin 2009;27:503–11.

Silberstein SD. Migraine and other headache disorders. Clin Updates Womens Health 2009;VIII (5):1–56.

74
Anemia

A 32-year-old African American woman with a history of gluten intolerance returns to the office for a prenatal visit at 28 weeks of gestation. In the first trimester, she was diagnosed with anemia. She had a hemoglobin level of 8.9 g/dL, hematocrit level of 27.3%, mean corpuscular volume of 78.5 fL, serum ferritin level 18.6 micrograms/L, and hemoglobin electrophoresis with 97% hemoglobin A. She has been taking oral ferrous sulfate twice daily since the first trimester. Repeat hemoglobin and hematocrit levels are 8.3 g/dL and 25.4%, respectively. The most appropriate next step in management is

(A) oral ferrous sulfate three times daily
(B) oral folic acid in addition to the current iron supplements
(C) subcutaneous erythropoietin
* (D) intravenous ferric gluconate
(E) blood transfusion

Anemia is a significant burden in antepartum patients and attention to the workup and treatment is important for healthy perinatal outcomes. The Centers for Disease Control and Prevention and the American College of Obstetricians and Gynecologists define anemia according to specific hemoglobin and hematocrit levels in each trimester (Table 74-1), based on the fifth percentile in a healthy, iron-supplemented reference population.

Iron-deficiency anemia is typically diagnosed with a hypochromic, microcytic anemia with evidence of reduced plasma iron levels and low iron stores, as indicated by low ferritin and high iron-binding capacity. Iron supplementation is advocated in all pregnant patients, with most prenatal vitamins supplying adequate amounts to fulfill daily elemental iron recommendations (27 mg per day). Iron-rich foods include clams, oysters, liver, beef, shrimp, turkey, enriched cereals, beans, and lentils. Foods that can inhibit iron absorption include soy and dairy products, coffee, and tea. Although spinach has a high iron content, it contains high levels of oxalate, which can paradoxically inhibit iron absorption.

Patients with iron-deficiency anemia require additional iron supplementation. Appropriate iron supplements include ferrous fumarate (106 mg of elemental iron per 325 mg tablet), ferrous sulfate (65 mg of elemental iron per 325 mg tablet), and ferrous gluconate (34 mg of elemental iron per 325 mg tablet). Addition of vitamin C or taking iron with orange juice can improve absorption. Folate does not improve iron absorption, but would be effective in patients with macrocytic anemia related to folate deficiency. Patients should be discouraged from taking supplements with antacids or using enteric-coated iron supplements, because both of these can reduce absorption.

TABLE 74-1. Reference Levels for Anemia in Pregnancy

	Hemoglobin Level (g/dL)	Hematocrit Level (%)
First Trimester	11	33
Second Trimester	10.5	32
Third Trimester	11	33

Modified from Anemia in pregnancy. ACOG Practice Bulletin No. 95. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008;112:201–7.

Patients who do not respond to iron therapy should be screened for coexisting diseases, malabsorption, nonadherence, or blood loss. Patients who do not tolerate or adhere to oral iron therapy are candidates for parenteral iron. Similarly, patients with malabsorption syndromes or severe iron deficiency are also suitable for such therapy. Oral therapy is recommended as an initial intervention because of ease of administration and lower risk of serious adverse effects. Response to iron is not expedited by parenteral administration. For the described patient, increasing her oral iron therapy is unlikely to correct her anemia.

Various different preparations are available for parenteral iron. Iron dextran use is discouraged given the high risk of adverse reactions, such as a 1% rate of anaphylaxis, which are not seen with ferric gluconate. The U.S. Food and Drug Administration reports the risk of life-threatening adverse drug events with ferric gluconate to be 0.9 per million doses; given this, a test dose is not necessary. Ferric gluconate is an iron salt that is compatible with normal saline and is given intravenously. Each 5 mL ampule contains 62.5 mg of elemental iron. Major infusion-related adverse effects are hypotension (if infused too fast), iron toxicity, or hypersensitivity (pruritus, rash).

Erythropoietin has been shown to reduce the time to achieve a target hemoglobin level in iron-deficient gravidas who also receive parenteral iron. Although one trial did not show an increase in adverse events compared with parenteral iron alone, erythropoietin is associated with increases in blood pressure. Erythropoietin should be reserved for use in patients on parenteral iron supplementation or those who require rapid correction of anemia. In the antepartum period, transfusion should be reserved for blood loss anemia or preoperatively in a patient with severe anemia.

Anemia in pregnancy. ACOG Practice Bulletin No. 95. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008; 112:201–7.

Recommendations to prevent and control iron deficiency in the United States. Centers for Disease Control and Prevention. MMWR Recomm Rep 1998;47:1–29.

75

Cholestasis and fetal risks

A 26-year-old woman, gravida 3, para 2, at 38 weeks of gestation comes to your office for an unscheduled prenatal care visit because of severe itching over her whole body, including her palms and soles. On physical examination, her blood pressure is normal and she has no right upper quadrant pain. Her urinalysis result is negative for protein. Three days later, her laboratory test results show increased serum bile acids (58 mmol/L), normal liver enzymes, and normal testing for hepatitis A, hepatitis B, and hepatitis C. The most appropriate next step in management is

(A) 24-hour urine collection for protein and creatine clearance
(B) biophysical profile testing
* (C) proceed to delivery
(D) diphenhydramine therapy
(E) amniocentesis for fetal lung maturity assessment

Severe pruritus combined with increased serum bile acids are consistent with a clinical diagnosis of intrahepatic cholestasis of pregnancy, which has an incidence of 0.01–0.5% in the United States. The condition occurs with greater frequency in women from Southern Asia and can be as high as 5% in Chilean women. Risk factors include a family history, multiple gestations, and the winter season. Greater than 80% of cases are diagnosed after 30 weeks of gestation. Bile acids are considered abnormal at levels of 14 mmol/L or greater; cases with bile acids greater than 40 mmol/L are considered severe.

Complications of untreated intrahepatic cholestasis of pregnancy include stillbirth (2–10%), preterm birth (15%), meconium stained amniotic fluid (45%), and nonreassuring fetal heart rate testing (5–15%).

Differential diagnosis includes other causes of liver disease, such as hepatitis, gallbladder disease, or hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome. In the described case, the findings of normal blood pressure and negative proteinuria make preeclampsia unlikely. Because her gestational age is 38 weeks, delivery should be considered to avoid risks of stillbirth. Thus, antenatal testing or symptomatic treatment are not optimal strategies.

If the gestational age at diagnosis was much earlier, medical treatment and close antenatal surveillance would be warranted. Common testing strategies include daily kick counts and nonstress testing (1–2 times per week). However, there are several reports of stillbirth within 24 hours of a reactive nonstress test. In severe cases (bile acids greater than 40 mmol/L), delivery should be undertaken by 37 weeks of gestation. No clinical trials have evaluated the optimal timing of delivery; the timing should be balanced by the severity of patient symptoms and risks of stillbirth versus iatrogenic delivery.

Data are limited on whether medical therapy improves perinatal outcomes. Treatment regimens include ursodeoxycholic acid (also known as ursodiol) as first line therapy. If ursodeoxycholic acid does not improve the patient's condition, S-adenosyl-L-methionine may be used. Both ursodeoxycholic acid and S-adenosyl-L-methionine are thought to decrease intestinal absorption of bile acids and enhance hepatocyte function. They also may facilitate the ability of the fetus to transport bile acids back to

maternal circulation. In addition, these medications have been shown to improve pruritus, and reduce bile acids and liver enzymes. Studies have not shown a decrease in rate of fetal death, but indirect evidence suggests that a lower level of bile acids is associated with less risk of stillbirth.

Burrows R, Clavisi O, Burrows E. Interventions for treating cholestasis in pregnancy. Cochrane Database of Systematic Reviews 2001, Issue 4. Art. No.: CD000493. DOI: 10.1002/14651858.CD000493; 10.1002/14651858.CD000493.

Glantz A, Marschall HU, Mattsson LA. Intrahepatic cholestasis of pregnancy: relationships between bile acid levels and fetal complication rates. Hepatology 2004;40:467–74.

Kenyon AP, Piercy CN, Girling J, Williamson C, Tribe RM, Shennan AH. Obstetric cholestasis, outcome with active management: a series of 70 cases. BJOG 2002;109:282–8.

Kenyon AP, Piercy CN, Girling J, Williamson C, Tribe RM, Shennan AH. Pruritus may precede abnormal liver function tests in pregnant women with obstetric cholestasis: a longitudinal analysis. BJOG 2001;108:1190–2.

Lammert F, Marschall HU, Glantz A, Matern S. Intrahepatic cholestasis of pregnancy: molecular pathogenesis, diagnosis and management. J Hepatol 2000;33:1012–21.

76

Severe rhesus disease in pregnancy

A 33-year-old woman, gravida 4, para 1, at 18 weeks of gestation presents for her first prenatal visit. She has a history of rhesus (Rh) alloimmunization with delivery of an anemic neonate that required exchange transfusion after birth in her most recent pregnancy. She reports certain paternity and that her husband is a known RhD homozygote. The most appropriate next step in management is to assess

(A) amniotic fluid ΔOD_{450}
(B) fetal hemoglobin level
* (C) fetal middle cerebral artery peak systolic velocity
(D) fetal RhD antigen status
(E) the maternal anti-D titer

Maternal alloimmunization is the result of an immune response in the mother to a foreign, paternally derived fetal red blood cell (RBC) antigen. In alloimmunized women, maternal immunoglobulin G antibodies can cross the placenta, bind to antigens present on fetal erythrocytes, and cause hemolysis, hydrops fetalis, and fetal death. In addition to the D antigen, more than 50 RBC antigens are associated with hemolytic disease of the newborn (Appendix D). Antibodies to D, c, and Kell are most commonly associated with severe hemolytic disease. Advances in Doppler ultrasonography and genetic technologies have favorably affected the outcome of maternal alloimmunization, but the condition remains a potential cause of perinatal morbidity and death.

Alloimmunization usually is detected during routine antibody screening at the first prenatal visit. Antibody identification and titer help determine the degree of alloimmunization. Titer values are reported as the integer of the greatest tube dilution with a positive agglutination reaction. For example, a titer of 8 is equivalent to a dilution of 1:8. A critical titer is one with a significant risk of hydrops fetalis that requires increased fetal surveillance. In most centers, the critical value for anti-D is between 1:8 and 1:32.

In a pregnancy in which RhD antibodies are detected, the next step is to assess paternal D antigen status. Further assessment and intervention are unnecessary when the father is D antigen-negative and paternity is certain. If the father is RhD positive or RhD status unknown, then maternal serum antibody titers are obtained every 2–4 weeks until a critical titer is reached or the woman gives birth. If the father is heterozygous and a critical maternal titer is reached, an amniocentesis is recommended to assess the fetal RhD genotype. Polymerase chain reaction on uncultured amniocytes reliably detects RhD-negative fetuses that are not at risk of anemia. Paternal homozygosity for the D antigen indicates an RhD-positive fetus and negates the need for amniocentesis for fetal antigen typing. Fetal RhD typing with the use of free fetal DNA in the maternal circulation also offers a viable option.

Serial maternal antibody titer assessment is not helpful once the critical titer is reached or in women with a

previously affected fetus or neonate. Ultrasonography is a vital tool for detection of anemia and management of affected pregnancies. The initial sonographic examination is performed to confirm fetal gestational age and to evaluate for signs of fetal compromise. Hydrops fetalis, or the abnormal accumulation of fluid in two or more fetal compartments, is a late finding with severe anemia.

Doppler ultrasonography is a noninvasive means of detecting fetal anemia through the identification of increased peak systolic velocity in the middle cerebral artery. Fetal anemia results in increased blood flow to the fetal brain as demonstrated by increased middle cerebral artery values. This technique has a reported sensitivity of 88–100% with a false-positive rate of 12–18% for the detection of moderate to severe fetal anemia. To obtain the peak systolic middle cerebral artery velocity, a transverse section through the fetal brain just caudal to the plane for the measurement of the biparietal diameter is chosen. The circle of Willis is identified and the Doppler gate is placed over the middle cerebral artery just as it arises from the carotid siphon. The angle of insonation should be 0 degrees and the anterior middle cerebral artery should be evaluated if possible (Fig. 76-1; see color plate).

Middle cerebral artery Doppler measurements are obtained serially and graphed based on gestational age. Norms for gestational age have been developed and values above 1.5 multiples of the median (MoM) are consistent with moderate to severe fetal anemia (Fig. 76-2). With values in this range, fetal blood sampling and transfusion for a fetal hematocrit less than 30% is performed. Middle cerebral artery Doppler outperformed amniocentesis in a prospective study and, as in the described scenario, is an appropriate first-line management tool in a center with trained personnel.

Amniocentesis is an invasive technique used to detect the presence of fetal anemia by measuring amniotic fluid bilirubin levels using spectral analysis at 450 nm (ΔOD_{450}). Fetal status is assessed by plotting the ΔOD_{450} measurement on either a Liley graph or on the Queenan curve (Fig. 76-3). The Queenan curve appears to be superior to the more traditional Liley curve. Serial amniocentesis to follow trends can be performed at 10-day to 2-week intervals. If values reach the intrauterine transfusion zone, then fetal blood sampling is indicated. A role for amniocentesis in the management of maternal alloimmunization still exists in certain scenarios. These include the lack of personnel trained in middle cerebral artery Doppler assessment and patients that are at or beyond 34 weeks of gestation because of the increased middle cerebral artery Doppler false-positive rate reported in women at or beyond this gestational age.

Fetal blood sampling is recommended for patients with elevated peak systolic middle cerebral artery velocities, elevated ΔOD_{450} values, or in cases of fetal ascites or hydrops fetalis. Fetal blood sampling is an invasive procedure that is associated with a 1–2% fetal loss rate. A spinal needle is guided into the umbilical vein near the placental insertion under direct ultrasonographic guidance. An initial hematocrit is obtained and a paralyzing agent may be administered. When fetal blood sampling is performed, blood should be available for an intravascular transfusion if the fetal hematocrit is less than 30%. The amount of blood transfused is based on the estimated fetal weight, the degree of anemia and the hematocrit of the donor unit. The final target hematocrit is 40–50%. An approach to clinical management of the sensitized woman is shown in Figure 76-4.

The use of anti-D immune globulin has led to a relative increase in the number of non-RhD alloimmunized pregnancies. In general, management of the patient with one of these clinically significant antibodies is similar to the care of RhD alloimmunized pregnant women. An important exception involves Kell alloimmunization, which often results in more severe fetal anemia than alloimmunization because of other erythrocyte antigens. Maternal Kell antibody titers and amniotic fluid ΔOD_{450} values are not as predictive of the degree of fetal anemia as with RhD sensitization but Doppler measurements appear to be accurate in predicting severe fetal anemia.

Management of alloimmunization during pregnancy. ACOG Practice Bulletin No. 75. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006;108:457–64.

Mari G, Deter RL, Carpenter RL, Rahman F, Zimmerman R, Moise KJ, et al. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloimmunization. Collaborative Group for Doppler Assessment of the Blood Velocity in Anemic Fetuses. N Engl J Med 2000;342:9–14.

Moise KJ. Fetal anemia due to non-rhesus-D red-cell alloimmunization. Semin Fetal Neonatal Med. 2008;13:207–14.

Moise KJ. Management of rhesus alloimmunization in pregnancy. Obstet Gynecol 2008;112:164–76.

Oepkes D, Seaward PG, Vandenbussche FP, Windrim R, Kingdom J, Beyene J, et al. Doppler ultrasonography versus amniocentesis to predict fetal anemia. N Engl J Med 2006;355:156–64.

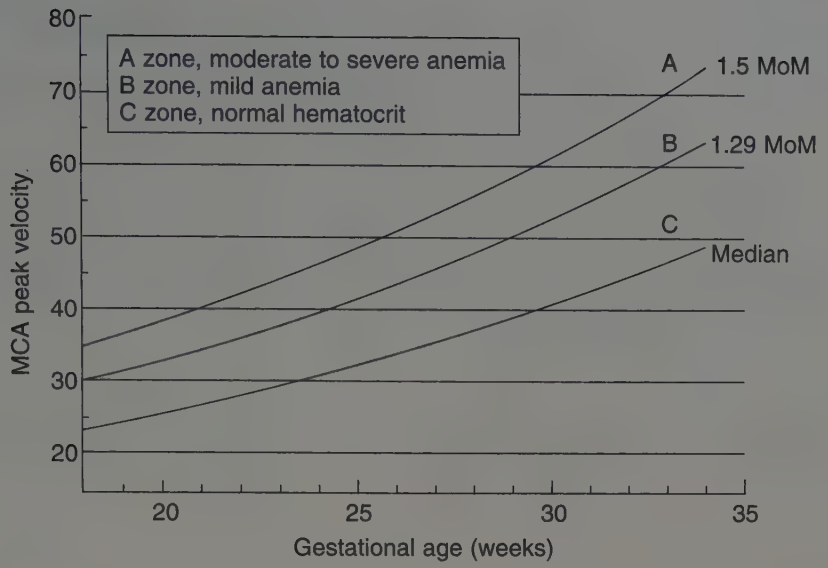


FIG. 76-2. Middle cerebral artery (MCA) Doppler graph based on gestational age. Abbreviation: MoM, multiple of the median. (Moise KJ. Management of rhesus alloimmunization in pregnancy. Obstet Gynecol 2008;112:164–76.)

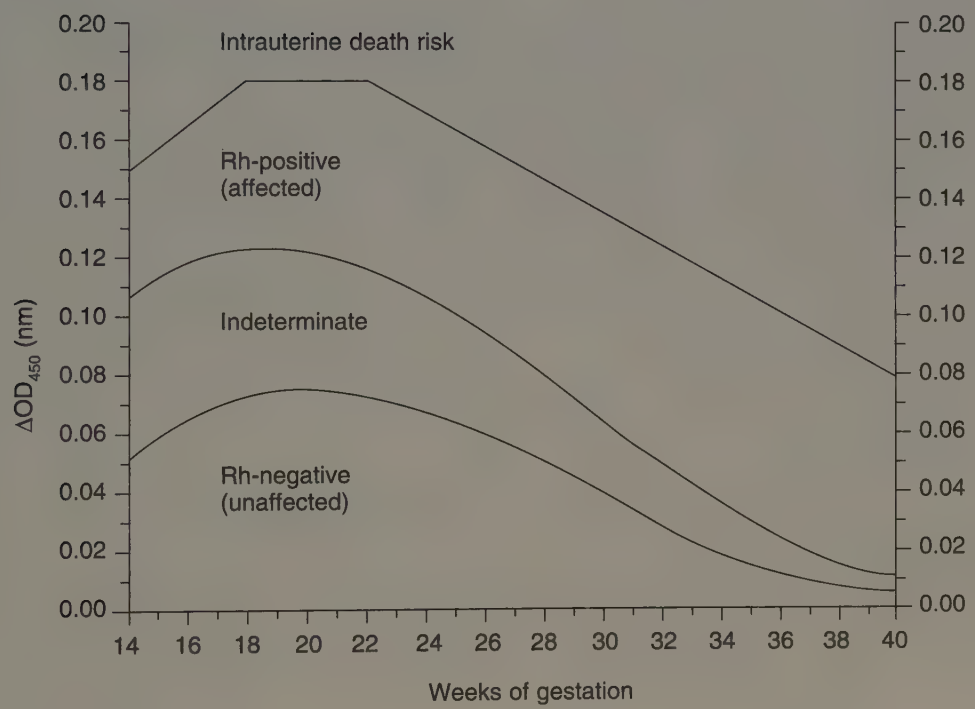


FIG. 76-3. Queenan curve for amniotic fluid ΔOD_{450} values. Abbreviations: ΔOD_{450}, delta optical density 450; Rh, rhesus. (Moise KJ. Management of rhesus alloimmunization in pregnancy. Obstet Gynecol 2008;112:164–76.)

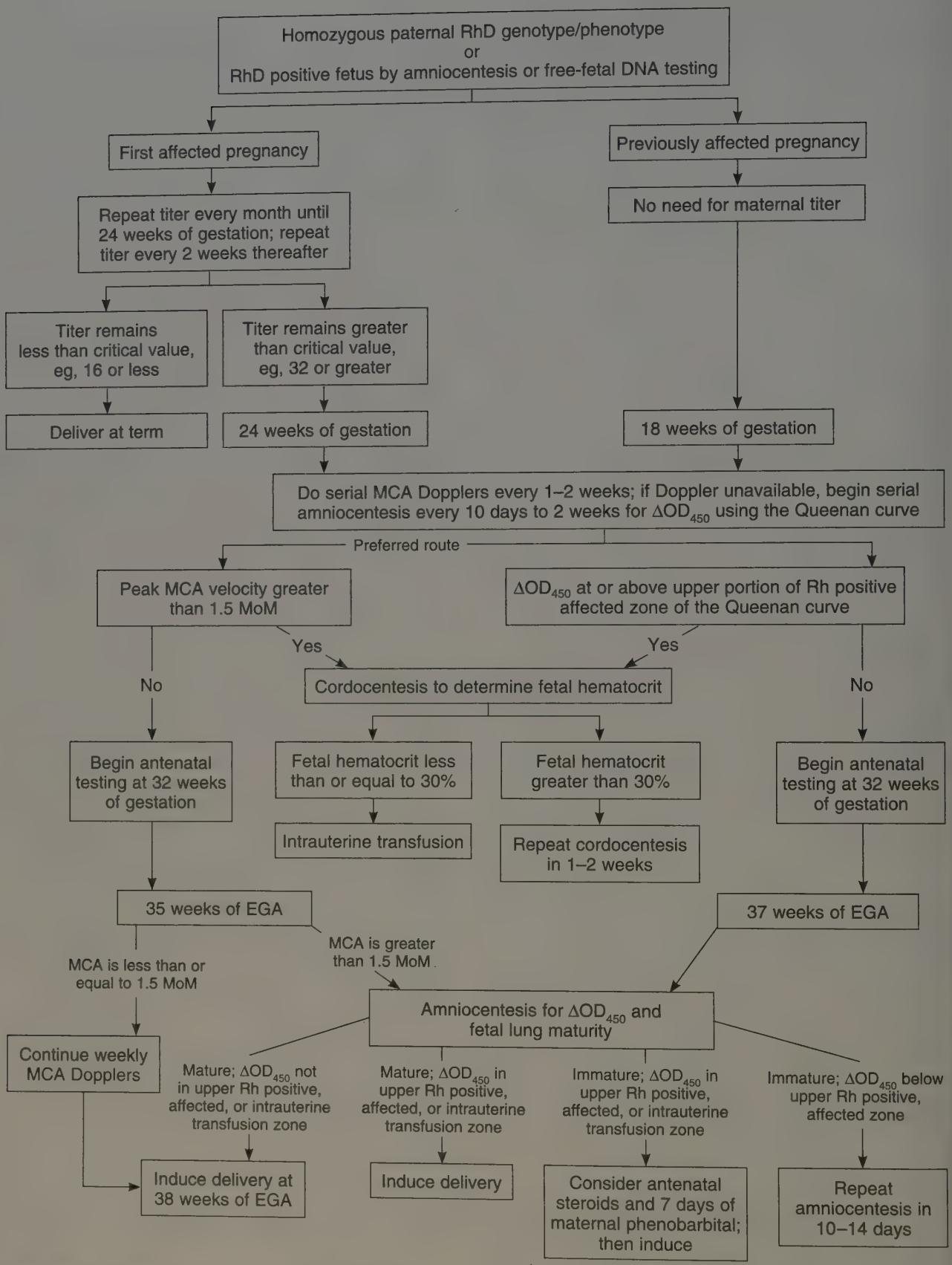

Homozygous paternal RhD genotype/phenotype
or
RhD positive fetus by amniocentesis or free-fetal DNA testing
First affected pregnancy
Previously affected pregnancy
Repeat titer every month until 24 weeks of gestation; repeat titer every 2 weeks thereafter
No need for maternal titer
Titer remains less than critical value, eg, 16 or less
Titer remains greater than critical value, eg, 32 or greater
Deliver at term
24 weeks of gestation
18 weeks of gestation
Do serial MCA Dopplers every 1–2 weeks; if Doppler unavailable, begin serial amniocentesis every 10 days to 2 weeks for ΔOD450 using the Queenan curve
Preferred route
Peak MCA velocity greater than 1.5 MoM
ΔOD450 at or above upper portion of Rh positive affected zone of the Queenan curve
Yes
Yes
No
Cordocentesis to determine fetal hematocrit
No
Begin antenatal testing at 32 weeks of gestation
Fetal hematocrit less than or equal to 30%
Fetal hematocrit greater than 30%
Begin antenatal testing at 32 weeks of gestation
Intrauterine transfusion
Repeat cordocentesis in 1–2 weeks
35 weeks of EGA
37 weeks of EGA
MCA is less than or equal to 1.5 MoM
MCA is greater than 1.5 MoM
Amniocentesis for ΔOD450 and fetal lung maturity
Continue weekly MCA Dopplers
Mature; ΔOD450 not in upper Rh positive, affected, or intrauterine transfusion zone
Mature; ΔOD450 in upper Rh positive, affected, or intrauterine transfusion zone
Immature; ΔOD450 in upper Rh positive, affected, or intrauterine transfusion zone
Immature; ΔOD450 below upper Rh positive, affected zone
Induce delivery at 38 weeks of EGA
Induce delivery
Consider antenatal steroids and 7 days of maternal phenobarbital; then induce
Repeat amniocentesis in 10–14 days

FIG. 76-4. Algorithm for overall clinical management of the sensitized gestation. Abbreviations: ΔOD_{450}, delta optical density 450; EGA, estimated gestational age; MCA, middle cerebral artery; MoM, multiple of the median; Rh, rhesus. (Moise KJ. Management of rhesus alloimmunization in pregnancy. Obstet Gynecol 2008;112:164–76.)

77

Tubal sterilization

A 36-year-old woman, para 1, at her 6-week postpartum visit wishes to discuss contraceptive options, including sterilization. She has a body mass index (calculated as weight in kilograms divided by height in meters squared [kg/m^2]) (BMI) of 52. Before her pregnancy, she experienced heavy menstrual bleeding for several years. The best management is

(A) vasectomy in her partner
* (B) levonorgestrel-releasing intrauterine system (levonorgestrel intrauterine device [IUD])
(C) hysteroscopic sterilization
(D) combination oral contraceptive
(E) laparoscopic tubal sterilization

Permanent sterilization accounts for 39% of contraceptive use in the United States. Approximately 28% of women opt for tubal sterilization and 11% depend on a partner's vasectomy for contraception. In the contraceptive counseling that obstetrician–gynecologists provide to patients, tubal sterilization is one of the most frequently discussed procedures and one of the most poorly understood by the public at large. The health care provider should discuss the risks versus benefits in the context of the patient's clinical situation in order to minimize unrealistic expectations.

Although vasectomy and tubal sterilization have never been compared in a comparative trial, the reported failure rates in this age group are similar: less than 1%. Vasectomy is a safer procedure than tubal sterilization because it does not require entry into the abdominal cavity. Data from the U.S. Collaborative Review of Sterilization Study, which examined nonhysteroscopic tubal sterilization, demonstrate that failures occur at the same rate annually over a 10-year period and that women younger than 35 years have somewhat higher failure rates than older women.

Several long-acting reversible contraceptives (LARCs) also have achieved pregnancy prevention rates that are similar to or better than tubal sterilization or vasectomy. These include the IUDs (copper T and levonorgestrel) as well as the implant. In addition, the levonorgestrel IUD is very effective as a treatment for women with abnormal bleeding. For patients whose primary interest is the efficacy of the procedure, the LARC options are similar to permanent sterilization and do not require surgery. The levonorgestrel IUD, which provides high efficacy and treatment for abnormal bleeding, would be the best option for the described patient.

Hysteroscopic sterilization is also an excellent option for an obese patient. It avoids abdominal surgery and often can be done under local anesthesia. However, because this patient also has a history of abnormal bleeding, it would not be the best option. Although the combination oral contraceptive can provide reasonable efficacy and can be used to control abnormal menstrual bleeding, the efficacy is lower than sterilization or the LARC methods. Further, because of the risk of venous thromboembolism, the use of the combination oral contraceptive is relatively contraindicated in obese women older than 35 years. Laparoscopic sterilization would be technically challenging to perform in this patient and would not be useful in the treatment of her abnormal bleeding.

Benefits and risks of sterilization. ACOG Practice Bulletin No. 46. American College of Obstetricians and Gynecologists. Obstet Gynecol 2003;102:647–58.

Intrauterine devices and intrauterine systems. ESHRE Capri Workshop Group. Hum Reprod Update 2008;14:197–208.

Long-acting reversible contraception: implants and intrauterine devices. Practice bulletin no. 121. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:184–96.

Peterson HB, Xia Z, Hughes JM, Wilcox LS, Tylor LR, Trussell J. The risk of pregnancy after tubal sterilization: findings from the U.S. Collaborative Review of Sterilization. Am J Obstet Gynecol 1996;174:1161–8; discussion 1168–70.

78

Hemolysis, elevated liver enzymes, and low platelet count syndrome

A 32-year-old woman, gravida 2, para 0, at 30 weeks of gestation with a dichorionic twin gestation presents with nausea and vomiting, right upper quadrant pain, and moderate vaginal bleeding. She has not experienced contractions or vaginal fluid leak. On examination, her blood pressure (BP) is 152/100 mm Hg and she appears in moderate distress with hyperreflexia and pitting edema of the lower extremities. Fetal tracing is reactive for both twins. Laboratory results show a platelet count of 64,000/mm^3, aspartate aminotransferase of 320 international units/L, alanine aminotransferase of 280 international units/L, creatinine of 1.3 mg/dL, lactate dehydrogenase of 700 international units/L, fibrinogen of 80 mg/dL, and prothrombin time of 18 seconds. In addition to administration of steroids, the most appropriate next step is

(A) delivery after completion of fetal lung maturity
(B) delivery at 34 weeks of gestation
(C) delivery after completion of steroids administration
* (D) immediate delivery

Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome is a manifestation of preeclampsia that complicates approximately 0.5–0.9% of all pregnancies and 10–20% of cases with severe preeclampsia. The pathophysiology involves microangiopathic hemolytic anemia and hepatic endothelial injury followed by platelet activation, aggregation, and consumption that result in ischemia and hepatocyte death.

Women may present with nonspecific symptoms or subtle signs of preeclampsia but the typical presentation includes acute onset of malaise, nausea, vomiting, and right upper quadrant or epigastric pain. Most women have hypertension and proteinuria, and commonly report headache. Laboratory criteria for HELLP syndrome include

- hemolysis defined as an abnormal peripheral smear, bilirubin greater than 1.2 mg/dL, or lactate dehydrogenase greater than 600 units/L.
- elevated liver enzymes defined as alanine aminotransferase and aspartate aminotransferase greater than 70 international units/L.
- low platelet count defined as 100,000/mm^3 or less.

Maternal death is seen in 1% of women with HELLP syndrome and significant morbidity is fairly common, eg, pulmonary edema (3–10%), acute renal failure (3–8%), disseminated intravascular coagulopathy (DIC) (15–20%), abruptio placentae (9–16%), liver hemorrhage or failure (approximately 1%), adult respiratory distress syndrome (approximately 1%), and eclampsia (4–9%). Perinatal death occurs in 7–20% and results from preterm delivery, fetal growth restriction, or placental abruption. Approximately 70% of neonates are born prematurely, which accounts for the significant rate of neonatal morbidity seen with this condition. The risk of adverse maternal and perinatal outcome is higher in women with HELLP syndrome compared with those with severe preeclampsia.

The clinical presentation and laboratory findings in women with HELLP syndrome overlap with several medical, surgical, and obstetric conditions (Box 78-1). Making an accurate diagnosis is critical because delivery will not improve the conditions listed, except for acute fatty liver of pregnancy. Hypertension or proteinuria may be absent in approximately 15% of cases, which compounds the difficulty in establishing a diagnosis.

BOX 78-1

Differential Diagnosis in Women With Hemolysis, Elevated Liver Enzymes, and Low Platelet Count Syndrome

- Acute fatty liver of pregnancy
- Thrombotic thrombocytopenic purpura
- Immune thrombocytopenic purpura
- Systemic lupus erythematosus
- Antiphospholipid syndrome
- Cholecystitis
- Fulminant viral hepatitis
- Acute pancreatitis
- Disseminated herpes simples
- Hemorrhagic or septic shock

Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynecol 2004;103:981–91.

The clinical course of women with HELLP syndrome is typically characterized by progressive and occasionally sudden deterioration in maternal status. Management involves assessment and stabilization of the maternal condition followed by fetal evaluation. Prompt delivery is indicated for gestational ages of 34 weeks or more, or earlier with the presence of multiorgan dysfunction, disseminated intravascular coagulation, liver infarction or hemorrhage, renal failure, suspected placental abruption, or abnormal fetal testing. Immediate delivery is recommended for the described patient because of the presence of disseminated intravascular coagulation and suspected placental abruption. Confirmation of fetal lung maturity is not necessary given the indication for immediate delivery. Magnesium sulfate for seizure prophylaxis should be instituted on admission and antihypertensive medications should be administered to keep systolic BP below 160 mm Hg or diastolic BP below 105 mm Hg.

Administration of the first dose of antenatal steroids is recommended on admission but a delay in delivery is not prudent. Maternal steroid administration has been shown to improve platelet count but does not affect the decision to deliver. Expectant management of HELLP syndrome is considered experimental.

Haram K, Svendsen E, Abildgaard U. The HELLP syndrome: clinical issues and management. A Review. BMC Pregnancy Childbirth 2009;9:8.

O'Brien JM, Barton JR. Controversies with the diagnosis and management of HELLP syndrome. Clin Obstet Gynecol 2005;48:460–77.

Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynecol 2004;103:981–91.

Woudstra DM, Chandra S, Hofmeyr GJ, Dowswell T. Corticosteroids for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD008148. DOI: 10.1002/14651858.CD008148.pub2.

79

Breast mass in pregnancy

A 29-year-old woman, gravida 3, para 2, at 34 weeks of gestation comes to your office with a newly discovered mobile, slightly tender 2-cm lump in her left breast that is confirmed on physical examination. There was no skin dimpling or axillary adenopathy and her right breast examination was normal. The rest of her history and physical examination are unremarkable. The best next step in management is

(A) initiate oral antibiotics
(B) mammography now
* (C) ultrasonography now
(D) postpartum mammography

Assessment and management of breast problems during pregnancy represent a special challenge for the health care provider. Physiologic changes can easily be confused with pathology, which can create concern for the patient and health care provider. A delay in diagnosis of malignancy also may represent a lost opportunity for early intervention. Most troublesome is that the common diagnostic tool of mammography poses a small risk of fetal radiation exposure and its accuracy may be compromised by the hormonal breast changes of pregnancy.

Breast cancer is the most common cancer in women. The mean age at diagnosis is 61 years. Only approximately 2% of cases of cancer occur in women aged 20–34 years and 10% in women aged 35–44 years. Although it is rare to develop cancer in pregnancy, breast cancer is the most common cancer seen during pregnancy; breast cancer occurs in 1 in 3,000 pregnancies. The most common mass observed in young women is a benign fibroadenoma. Other benign masses include benign cysts and, in the postpartum period, galactoceles or milk-filled cysts.

Fibroadenomas are defined as benign solid tumors that contain glands and fibrous tissues. They most commonly occur in women aged 15–35 years. Fibroadenomas can be diagnosed with a fair amount of certainty using a combination of imaging with or without biopsy. Surgical excision is not required and close follow-up can be offered. *Galactoceles* are defined as milk-containing cysts, which develop when obstruction of the breast duct occurs during lactation. They can be aspirated if necessary or followed.

Ultrasonography is the first diagnostic test when a breast mass is discovered in a younger woman because of the increased likelihood that the mass is benign. The

ultrasonographic appearance of a fibroadenoma is well described as a circumscribed homogeneous oval. Ultrasonography is also a more appropriate test because it spares the patient the radiation exposure associated with conventional mammography, and is less expensive when compared with either magnetic resonance imaging or computerized tomography scan. In this young pregnant patient, ultrasonography is the best next step.

Mammography is not indicated as a first diagnostic test in young women and often cannot reliably distinguish between a fibroadenoma, cyst, or carcinoma. Mammography also may be diagnostically limited because of the association between dense breast tissue and young age and pregnancy. However, if ultrasonography is inconclusive or further workup is required, mammography can be performed in pregnancy with proper shielding. Mammography evaluates the entire breast and can survey both breasts. If there continues to be concern that a breast mass is malignant, fine needle aspiration (using a thin needle) or core biopsy (using a larger needle) can be performed to obtain a definitive diagnosis.

The risk of breast cancer in pregnancy is low; however, the risk is not zero and, thus, masses detected in pregnancy need to be evaluated at the time of discovery. To wait until the postpartum period to evaluate a breast mass may jeopardize the chance of diagnosing and treating early cancer.

Mastitis usually is seen in lactating women and, even in that group, the incidence of a breast abscess is less than 10%. Oral antibiotics would be indicated if there was a suspicion of an infected breast mass or abscess. In the described patient, there was no fever or erythema noted on examination and infection was not suspected.

Hartmann LC, Sellers TA, Frost MH, Lingle WL, Degnim AC, Ghosh K, et al. Benign breast disease and the risk of breast cancer. N Engl J Med 2005;353:229–37.

Robbins J, Jeffries D, Roubidoux M, Helvie M. Accuracy of diagnostic mammography and breast ultrasound during pregnancy and lactation [published erratum appears in AJR Am J Roentgenol 2011;196:1237]. AJR Am J Roentgenol 2011;196:716–22.

Sabate JM, Clotet M, Torrubia S, Gomez A, Guerrero R, de las Heras P, et al. Radiologic evaluation of breast disorders related to pregnancy and lactation. Radiographics 2007;27 Suppl 1:S101–24.

Son EJ, Oh KK, Kim EK. Pregnancy-associated breast disease: radiologic features and diagnostic dilemmas. Yonsei Med J 2006;47:34–42.

80

Postpartum fever

A postpartum ward nurse calls to tell you that the patient you delivered at term 12 hours ago has a temperature of 38.3°C (101°F). She had a cesarean delivery with no complications. She lost an estimated 800 cc of blood. You review her chart and medical history. The best next step in management is

(A) complete blood count, urinalysis, and chest X-ray
(B) acetaminophen and observation
(C) broad-spectrum antimicrobial coverage
* (D) examination of the patient

There are several possible etiologies for postpartum fever including, but not limited to, urinary tract infection, pulmonary problems (eg, atelectasis), uterine infection (ie, endometritis), wound infection, and venous thromboembolism. Before any laboratory or radiologic workup, examination of the patient is the first step in management after a review of the patient's history. For example, the diagnosis of postpartum endometritis is based on the presence of two or more of the following: temperature greater than 37.9°C (100.3°F) at least twice, 6 hours or more apart; fundal tenderness; tachycardia (heart rate greater than 100 beats per minute); and foul-smelling lochia. All of these findings may be made on a physical examination. Endometrial cultures are usually not necessary.

Many factors may lead to overtreatment of febrile morbidity including patient and family concerns in regard to treatment of a fever. Such concerns can lead to a reflex response on the part of some health care providers to behave as though "fever" were synonymous with "infection." This is not the case; overtreatment carries rare but concerning risks, such as anaphylaxis. It raises public health issues in regard to resistant organisms. Therefore, it is incumbent on the health care provider to evaluate each fever within the context of the overall patient status, including first history and physical examination.

A full laboratory and X-ray workup of a fever within the first 24 hours of delivery is rarely useful in determining the source of the fever. White blood cell count will almost certainly be elevated by pregnancy and also by the surgery, particularly if the patient labored before the cesarean delivery. The white blood cell count also might show the classic "left shift" regardless of presence or absence of infection. It is thus nondiscriminatory. Urinalysis and urine culture may be helpful in cases where the physical examination is unremarkable, but may require catheterization in order to avoid contamination by lochia, and should be reserved for persistent fever. Chest X-ray quality is not indicated unless there are physical findings that suggest a pulmonary source. Acetaminophen is a helpful intervention for reducing fever; however, acetaminophen should not be initiated without first doing a careful evaluation of the patient.

Based on several randomized trials, this patient should have received a preincision dose of antibiotic (eg, cephalexin) before the cesarean delivery. This is an excellent choice for suppression of microbes at the site of the incision and has been shown to decrease subsequent postoperative infections. Use of broad-spectrum antimicrobials postoperatively should be reserved for treatment only once a specific diagnosis has been made, and not just for an isolated fever within the first 24 hours postpartum. If the diagnosis of endometritis is made by repeated elevated temperatures and physical examination findings, appropriate treatment with broad-spectrum antibiotics (eg, gentamicin and clindamycin) is indicated. The precondition for treatment is assessment of the fever source.

De Palma RT, Leveno KJ, Cunningham FG, Pope T, Kappus SS, Roark ML, et al. Identification and management of women at high risk for pelvic infection following cesarean section. Obstet Gynecol 1980;55:185S–92S.

Fanning J, Brewer J. Delay of hospital discharge secondary to postoperative fever—is it necessary? J Am Osteopath Assoc 2002;102:660–1.

Schwandt A, Andrews SJ, Fanning J. Prospective analysis of a fever evaluation algorithm after major gynecologic surgery. Am J Obstet Gynecol 2001;184:1066–7.

81

Peripartum cardiomyopathy

A patient presents for preconception counseling. She had peripartum cardiomyopathy with an ejection fraction of 20% after her most recent delivery. She took a β-blocker, an angiotensin-converting enzyme (ACE) inhibitor, and a diuretic for 2 years and her heart fully recovered. Her most recent echocardiogram revealed an ejection fraction of 60%. She wants to know her recurrence risk of cardiomyopathy in a future pregnancy. You advise her that her recurrence risk is approximately

(A) less than 1%
(B) 5–15%
* (C) 20–30%
(D) 40–50%
(E) 60–70%

Peripartum cardiomyopathy is a rare condition with an incidence of approximately 1 in 3,000–4,000 live births in the United States. Risk factors for developing the condition are advanced maternal age, multiparity, African American race, multiple gestations, hypertensive disorders of pregnancy, and the use of tocolytics. The diagnostic criteria for peripartum cardiomyopathy include all of the following:

- Cardiac failure within the last month of pregnancy or 5 months postpartum
- Absence of demonstrable preexisting cardiac disease
- Absence of an identifiable cause for cardiac failure
- Left ventricular systolic dysfunction demonstrated by classic echocardiographic criteria, such as ejection fraction less than 45% or a fractional shortening less than 30%, or both

At presentation, patients have symptoms that suggest congestive heart failure, such as shortness of breath on exertion, nocturnal dyspnea, cough, and pedal edema. During the last month of pregnancy, the patient may experience similar symptoms without any underlying cardiac pathology. The health care provider can distinguish the difference on physical examination. Patients with congestive heart failure usually have a heart rate greater than 100 beats per minute, elevated jugular venous pressure, a third heart sound, and rales at the base of the lungs. The diagnosis is confirmed with echocardiography.

Medical management of peripartum cardiomyopathy is similar to the management of the other forms of nonischemic dilated cardiomyopathy. The aim of medical therapy is to reduce fluid and salt intake, increase cardiac contractility, reduce cardiac preload and afterload, prevent complications (eg, arrhythmias and thromboembolism), and promote cardiac remodeling. Fluid and salt restriction is advisable. Bed rest is not recommended unless the patient can not tolerate any physical activity.

Diuretics are initiated to reduce preload and relieve pulmonary edema. Nitrates and hydralazine may be used to reduce afterload; ACE inhibitors or angiotensin receptor blockers should be given to help with cardiac remodeling. However, if the peripartum cardiomyopathy develops before delivery, ACE inhibitors and angiotensin receptor blockers are contraindicated because of the risk of fetal renal failure, which is irreversible. A β-blocker should be initiated to decrease the risk of arrhythmia and sudden death, and to improve the long-term prognosis. Anticoagulation should be considered in women with peripartum cardiomyopathy, especially if the ejection fraction is less than 35% and the ventricles are severely dilated. The patient should be monitored regularly to ascertain the response to treatment. Monitoring includes clinical symptoms and echocardiography.

Approximately 30–50% of patients with peripartum cardiomyopathy will completely recover. Despite full recovery of left ventricular function by echocardiography, a dobutamine stress test may demonstrate reduced contractile reserve. If the patient's left ventricular function has not returned to normal at 6 months, the prognosis for a full recovery is much less likely. However, some improvements in cardiac function have been observed for up to 2–3 years. If a patient shows progressive deterioration of left ventricular function, the patient should have an early evaluation for a heart transplant.

Ideally, every woman with a prior peripartum cardiomyopathy will have preconception counseling. After a full recovery is documented, ACE inhibitors and β-blockers usually are continued for 1 year. Echocardiography should be performed to assess left ventricular function and a dobutamine stress test should be considered. Maternal outcomes in subsequent pregnancies in women with peripartum cardiomyopathy are shown in Table 81-1. Women who have a full recovery have a recurrence risk in a subsequent pregnancy of approximately 20%. A patient who

TABLE 81-1. Maternal Outcomes of Subsequent Pregnancies in Women with Peripartum Cardiomyopathy

Heart Function	Recurrence Risk of PPCM (%)	Maternal Mortality Risk (%)
Recovered (EF greater than 50%)	21	0
Persistent dysfunction	44	19

Abbreviations: EF, ejection fraction; PPCM, peripartum cardiomyopathy.

does not fully recover left ventricular function should be counseled strongly to avoid subsequent pregnancy as the maternal mortality is significant.

Elkayam U, Tummala PP, Rao K, Akhter MW, Karaalp IS, Wani OR, et al. Maternal and fetal outcomes of subsequent pregnancies in women with peripartum cardiomyopathy. N Engl J Med 2001;344:1567–71.

Grewal J, Siu SC, Ross HJ, Mason J, Balint OH, Sermer M, et al. Pregnancy outcomes in women with dilated cardiomyopathy. J Am Coll Cardiol 2009;55:45–52.

Moioli M, Valenzano Menada M, Bentivoglio G, Ferrero S. Peripartum cardiomyopathy. Arch Gynecol Obstet 2010;281:183–8.

Pearson GD, Veille JC, Rahimtoola S, Hsia J, Oakley CM, Hosenpud JD, et al. Peripartum cardiomyopathy: National Heart, Lung, and Blood Institute and Office of Rare Diseases (National Institutes of Health) workshop recommendations and review. JAMA 2000;283:1183–8.

Pyatt JR, Dubey G. Peripartum cardiomyopathy: current understanding, comprehensive management review and new developments. Postgrad Med J 2011;87:34–9.

Sliwa K, Tibazarwa K, Hilfiker-Kleiner D. Management of peripartum cardiomyopathy. Curr Heart Fail Rep 2008;5:238–44.

82

Induction of labor

A 31-year-old woman, gravida 3, para 2, presents for decreased fetal movement at 39 3/7 weeks of gestation. She has a history of one prior spontaneous vaginal delivery followed by a primary low-transverse cesarean delivery for breech presentation. You have monitored her pregnancy and have discussed her option of trial of labor after cesarean delivery (TOLAC). She favors a vaginal delivery for this pregnancy and also desires more children in the future. Nonstress testing demonstrates a reactive fetal heart rate with baseline of 130 beats per minute. Ultrasonography shows vertex cephalic presentation and oligohydramnios with an amniotic fluid index of 1.5 cm. Vaginal examination reveals a cervix that is 1 cm dilated, 20% effaced, posterior, and soft. Fetal station is –3. In this scenario, the most appropriate next step in management is

(A) vaginal misoprostol
(B) intravenous oxytocin
* (C) transcervical Foley balloon
(D) repeat cesarean delivery
(E) expectant management

Trial of labor after cesarean delivery is seen as a reasonable option for some patients who wish to avoid a repeat cesarean delivery, with successful TOLAC possible in 60–80% of appropriate candidates. The opportunity for planned TOLAC should be presented to eligible patients and should be discussed openly and continuously during the antepartum period.

Successful TOLAC can provide multiple individual and global benefits:

- Fulfilling a patient's possible preferences for vaginal delivery
- Faster recovery after successful TOLAC (compared with repeat cesarean delivery)
- Decreased risk of complications resulting from surgery
- Decreased risk of complications for future pregnancies
- Decrease in breathing problems for babies who experience labor
- Decrease in overall cesarean delivery rate

However, patients with a prior cesarean delivery are at increased risk of complications related to labor, specifically uterine rupture, which is associated with both maternal and fetal risks. Maternal risks associated with uterine rupture include hemorrhage, hysterectomy, operative injury, infection, anemia, and transfusion. Fetal risks in these circumstances include hypoxic injury and death.

The risk of uterine rupture is lowest in patients who have a repeat cesarean delivery before the onset of labor. It is generally believed that the risk of uterine rupture during a spontaneously occurring trial of labor is approximately 1 in 200 (0.5%). However, the risk of uterine rupture depends on scar location and type, the number of prior incisions, and the type of labor. This low absolute risk may be acceptable to many patients, particularly those motivated by the benefits of vaginal birth after cesarean delivery.

Although uterine rupture may occur spontaneously in the antepartum period in any patient with a prior cesarean delivery, and the risk increases with spontaneous labor, induced labor adds even greater risk. Chances of uterine rupture in general are increased twofold to fivefold when induction or augmentation of labor is required (Table 82-1), although this risk may be concentrated in patients who do not have a prior vaginal delivery. When inducing labor in a patient with prior cesarean delivery, documentation should include a notation that the patient was informed and accepts this increased risk.

In attempts at vaginal birth after cesarean delivery, oxytocin should be used judiciously. However, the patient with the unfavorable cervix presents a particular challenge, as oxytocin is less effective for cervical ripening. Ripening with prostaglandins or mechanical methods reduces the cesarean delivery rate compared with oxytocin alone in patients with an unfavorable cervix. Misoprostol (prostaglandin E_1) is associated with an unacceptably increased risk of uterine rupture and should not be used in third-trimester cervical ripening or induction in patients who have had a prior cesarean delivery or major uterine surgery.

Data suggest that transcervical Foley catheter for cervical ripening is not associated with the same risks of

TABLE 82-1. Labor Type and Risk of Uterine Rupture

	Absolute Risk of Uterine Rupture per 1,000	Relative Risk of Uterine Rupture (95% CI)	Odds Ratio of Uterine Rupture (95% CI)
Planned repeat cesarean delivery	0–1.6	1.0 (Reference)	–
Spontaneous labor	3.6–5.2	3.3 (1.8–6.0)	1.0 (Reference)
Induction without prostaglandins	7.7–8.9	4.9 (2.4–9.7)	2.5 (1.3–4.8)
Induction with prostaglandins	14.0–24.5	15.6 (8.1–30.0)	4.0 (2.0–7.8)

Adapted from Lydon-Rochelle M, Holt VL, Easterling TR, Martin DP. Risk of uterine rupture during labor among women with a prior cesarean delivery. N Engl J Med 2001;345:3–8 *and* Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW, et al. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. N Engl J Med 2004;351:2581–9.

uterine rupture as prostaglandins. The advantages of balloon catheter ripening over the pharmacologic modalities are low cost, longer dose interval, decreased risk of uterine tachysystole, and potential decreased need for fetal monitoring. Consequently, transcervical balloon catheter ripening is a viable option for TOLAC candidates with an unfavorable cervix.

For this patient, with oligohydramnios at term, expectant management to await spontaneous labor should not be advocated, given the risk of adverse outcome associated with oligohydramnios.

Induction of labor. ACOG Practice Bulletin No. 107. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:386–97.

Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW, et al. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. N Engl J Med 2004;351:2581–9.

Lydon-Rochelle M, Holt VL, Easterling TR, Martin DP. Risk of uterine rupture during labor among women with a prior cesarean delivery. N Engl J Med 2001;345:3–8.

Vaginal birth after previous cesarean delivery. Practice Bulletin No. 115. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:450–63.

83

Maternal human immunodeficiency virus

Pregnant women should be offered human immunodeficiency virus (HIV) testing as part of the routine package of prenatal laboratory tests. Women with high-risk behavior factors who require an additional third-trimester test possess the characteristic of

(A) homelessness
(B) hepatitis C virus
(C) emigrant from a high-prevalence region
* (D) residence in a high-prevalence area

Today, it is accepted practice to screen pregnant women for HIV. The American College of Obstetricians and Gynecologists states, "All pregnant women should be screened for HIV infection as early as possible during each pregnancy. . . as part of the routine panel of prenatal tests unless they decline (opt-out screening)."

The interruption of mother-to-child transmission is one of the great public health triumphs of the past two decades. In the absence of antiretroviral therapy, 25% of pregnant women who are HIV positive will give birth to infants who are HIV positive, but with currently available antiviral regimens that risk is as low as 1–2%. The treatment strategy is a three-part regimen:

1. Multiple highly active antiretroviral drugs are administered to the woman during pregnancy
2. Zidovudine is administered during labor (and her other medications continued)
3. The newborn is treated with zidovudine for 6 weeks

If the mother is not treated during pregnancy, mother-to-child transmission can still be lessened with maternal treatment during labor plus treatment of the newborn (transmission rate is 9–20% in studies done in Africa). There is even some benefit with treatment of the newborn alone, preferably instituted within 6–12 hours after birth (transmission rate in African studies is 12–20%).

A prerequisite to treatment is effective screening. Both the American College of Obstetricians and Gynecologists and the Centers for Disease Control and Prevention (CDC) recommend HIV screening as early as feasible during pregnancy. State laws vary about opt-in versus opt-out testing, the degree of pretest and posttest counseling required, and consent requirements, all of which can present barriers to screening. State-specific legal requirements are available from the National HIV/AIDS Clinicians' Consultation Center (http://www.nccc.ucsf.edu/docs/Perinatal_QRG.pdf). Women who do not have prenatal documentation of HIV status should be offered another opportunity to learn their serostatus when they present in labor. Women who decline prenatal HIV screening have been shown to be much more likely to be HIV positive than women who agree to screening. Other women may have had no prenatal care or may have missed laboratory testing. In an attempt to capture this nonscreened group, rapid HIV testing has been instituted at many labor and delivery units. The advent of rapid HIV tests with a turnaround time of less than 2 hours allows for intrapartum and neonatal treatment if a positive result is returned. Rapid testing on labor and delivery units is highly acceptable to women who qualify, and test performance is excellent: 100% negative predictive value and 90% positive predictive value.

When the rapid test is positive at the time of admission for labor, the woman should begin intrapartum prophylaxis with zidovudine while confirmatory testing is performed. The newborn also should receive treatment unless the confirmatory Western blot result is negative several days later. Antepartum identification and initiation of treatment is associated with lower mother-to-child transmission rates than beginning treatment during the intrapartum period. In addition, women who are HIV negative at the time of initial prenatal testing may still acquire HIV during the pregnancy, and those cases are at more than 10-fold higher risk of maternal transmission than if HIV seropositivity was known prenatally.

Thus, there is a place for a second HIV screening test during pregnancy. The CDC recommends third-trimester testing for women who meet any of the criteria listed in Box 83-1. Although the CDC recommends that women in these high-risk categories be screened with a second HIV test before 36 weeks of gestation, even women who do not fall within these categories may be screened a second time. A repeat test performed in the third trimester is cost-effective even in areas of low HIV prevalence. The American College of Obstetricians and Gynecologists states that women who are candidates for third-trimester testing should have either rapid or conventional testing performed prenatally, rather than wait to have a rapid

BOX 83-1

The Centers for Disease Control and Prevention Recommends Third-Trimester Human Immunodeficiency Virus Testing for Women Who Meet Any of the Following Criteria:

- Women who are at high risk for acquiring HIV, such as women with new or multiple sex partners during the pregnancy, women who engage in prostitution, women who are injection-drug users, and women who are sex partners of HIV-infected individuals or injection-drug users
- Women who receive health care in facilities in which prenatal screening identifies a seroprevalence of at least 1 per 1,000
- Women who receive health care in jurisdictions with an increased incidence of HIV in women of reproductive age; the list of jurisdictions is not reproduced here but is extensive. The CDC cutoff for an increased incidence of HIV in reproductive-aged women is greater than 17 HIV cases per 100,000 person-years; jurisdictions in which this threshold is met have been delineated. See http://www.cdc.gov/hiv/testing/HIVStandardCare/resources/brochures/MMWR-Annotated%20508C_Full.pdf.
- Women who have signs or symptoms consistent with acute HIV infection

Abbreviations: CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus.

Branson BM, Handsfield HH, Lampe MA, Janssen RS, Taylor AW, Lyss SB, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. Centers for Disease Control and Prevention. MMWR Recomm Rep 2006;55:1,17; quiz CE1–4.

test performed during labor and delivery. The National Perinatal HIV Hotline (1-888-448-8765) provides free 24-hour telephone consultation on questions of perinatal HIV care.

Boxall EH, Smith N. Antenatal screening for HIV; are those who refuse testing at higher risk than those who accept testing? J Public Health (Oxf) 2004;26:285–7.

Branson BM, Handsfield HH, Lampe MA, Janssen RS, Taylor AW, Lyss SB, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. Centers for Disease Control and Prevention. MMWR Recomm Rep 2006;55:1,17; quiz CE1–4.

Bulterys M, Jamieson DJ, O'Sullivan MJ, Cohen MH, Maupin R, Nesheim S, et al. Rapid HIV-1 testing during labor: a multicenter study. Mother–Infant Rapid Intervention At Delivery (MIRIAD) Study Group. JAMA 2004;292:219–23.

Mseleku M, Smith TH, Guidozzi F. HIV seropositive in pregnant South African women who initially refuse routine antenatal HIV screening. BJOG 2005;112:370–1.

National HIV/AIDS Clinicians' Consultation Center. Perinatal quick reference guide: a guide to states' perinatal HIV testing laws for clinicians. Compendium of state HIV testing laws. San Francisco (CA): NCCC; 2011. Available at: http://www.nccc.ucsf.edu/docs/Perinatal_QRG.pdf. Retrieved June 11, 2012.

Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Washington, DC: United States Department of Health and Human Services; 2011. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Retrieved June 10, 2012.

Prenatal and perinatal human immunodeficiency virus testing: expanded recommendations. ACOG Committee Opinion No. 418. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008;112:739–42.

84

Hypertension in pregnancy

A 30-year-old multiparous woman with a history of chronic hypertension discontinued her usual medications when she learned she was pregnant. At her prenatal visit at 22 weeks of gestation, her blood pressure (BP) is 148/90 mm Hg. Urine dipstick shows no protein. She reports no other medical problems. The best next step in her management is

* (A) no medication
(B) methyldopa
(C) labetalol
(D) magnesium sulfate

Hypertension is a common medical condition that coexists with or complicates pregnancy. *Chronic hypertension in pregnancy* is defined as hypertension that predates the onset of pregnancy or is diagnosed before 20 weeks of gestation. Although physicians typically think of hypertension as either mild (systolic BP 140 mm Hg or greater, diastolic BP 90 mm Hg or greater) or severe (systolic BP 180 mm Hg or greater, diastolic BP 110 mm Hg or greater), the current classification system, as advocated in the National Institutes of Health's Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), describes hypertension as stage 1 (140–159/90–99 mm Hg) or stage 2 (160/100 mm Hg or greater). Control of hypertension over years is important in limiting mortality from stroke, heart failure, and other cardiovascular events.

There are several classification schemes for hypertension during pregnancy. Chronic hypertension is not the same disorder as preeclampsia and does not have the same maternal or fetal outcomes, although 10–20% of women with chronic hypertension will develop superimposed preeclampsia. Lesser degrees of hypertension are typically well tolerated in pregnancy. The rate of stillbirth in the United States in women with hypertension ranges from 1–3 per 1,000 at term. The overall risk of stillbirth in high-income countries, including preterm pregnancies and, therefore, inevitably women with more severe disease, is 2–3 times higher in women with hypertension than without hypertension, according to a recent meta-analysis.

The incidence of fetal growth restriction increases in hypertensive pregnancy. With preexisting (chronic) hypertension or nonproteinuric gestational hypertension, the probability of fetal growth restriction is estimated at approximately 15%. It is unclear, however, whether impaired fetal growth is due to disease or treatment. The placenta does not regulate itself, so drugs that lower maternal blood pressure inevitably have the potential to lower uteroplacental perfusion as well. Several clinical trials suggest higher rates of fetal growth restriction with the use of β-blockers compared with placebo. This effect has not been clearly demonstrated with other classes of drugs, but a meta-regression of 15 trials does suggest that with greater treatment-induced declines in mean arterial pressure, the proportion of small for gestational age infants increases regardless of the agent used.

Controversy exists in regard to optimal BP during pregnancy, as well as the optimal agent for control of hypertension in pregnancy. A pilot study of "tight" versus "less tight" BP control during pregnancy, where the target diastolic BP was either 85 mm Hg or 100 mm Hg, showed a trend toward improved perinatal outcomes with less tight control. A multicenter randomized controlled trial, the Control of Hypertension in Pregnancy Study, is underway with a target of recruiting more than 1,000 women. In a Cochrane review of 46 trials involving more than 4,000 women with "mild to moderate hypertension" (BP of 140–169/90–109 mm Hg), neither the rate of stillbirth nor small for gestational age was affected when mothers were treated with an antihypertensive agent, compared with placebo. The probability of progression to severe hypertension was, however, halved when women received an antihypertensive drug. The effects of this change in pregnancy are unknown. At this time, it is unclear whether one agent is preferable to another. It does appear, however, that beginning an antihypertensive drug confers no benefit to either the mother or her fetus unless her hypertension is severe.

Magnesium has no antihypertensive effect. Its only use is in reducing the risk that preeclampsia will progress to eclampsia. Although both labetalol and methyldopa are safe drugs to use in pregnancy, the degree of hypertension in this patient does not warrant pharmacologic treatment.

Abalos E, Duley L, Steyn DW, Henderson-Smart DJ. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.: CD002252. DOI: 10.1002/14651858.CD002252.pub2; 10.1002/14651858.CD002252.pub2.

Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JLJ, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee [published erratum appears in JAMA 2003;290:197]. JAMA 2003;289:2560–72.

Chronic hypertension in pregnancy. ACOG Practice Bulletin No. 29. American College of Obstetricians and Gynecologists. Obstet Gynecol 2001;98:177–85.

Diagnosis and management of preeclampsia and eclampsia. ACOG Practice Bulletin No. 33. American College of Obstetricians and Gynecologists. Obstet Gynecol 2002;99:159–67.

Flenady V, Koopmans L, Middleton P, Froen JF, Smith GC, Gibbons K, et al. Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. Lancet 2011;377:1331–40.

Hutcheon JA, Lisonkova S, Magee LA, Von Dadelszen P, Woo HL, Liu S, et al. Optimal timing of delivery in pregnancies with pre-existing hypertension. BJOG 2011;118:49–54.

Magee LA, Abalos E, von Dadelszen P, Sibai B, Walkinshaw SA. Control of hypertension in pregnancy. CHIPS Study Group. Curr Hypertens Rep 2009;11:429–36.

Magee LA, von Dadelszen P, Chan S, Gafni A, Gruslin A, Helewa M, et al. The Control of Hypertension In Pregnancy Study pilot trial. CHIPS Pilot Trial Collaborative Group. BJOG 2007;114:770, e13–20.

von Dadelszen P, Ornstein MP, Bull SB, Logan AG, Koren G, Magee LA. Fall in mean arterial pressure and fetal growth restriction in pregnancy hypertension: a meta–analysis. Lancet 2000;355:87–92.

85

Twin–twin transfusion syndrome

A 34-year-old woman has a known twin pregnancy. Her referring physician noted discordant growth on 20-week ultrasonography. The set of ultrasonographic findings most consistent with twin–twin transfusion syndrome is

(A) twin peak sign, twin B with fetal growth restriction, and renal anomaly
(B) twin peak sign, decreased amniotic fluid twin B, and hydramnios twin A
(C) thin dividing membrane, twin B with fetal growth restriction, and renal anomaly
* (D) thin dividing membrane, decreased amniotic fluid twin B, and hydramnios twin A

Twin–twin transfusion syndrome takes place almost exclusively with monochorionic placentation. It is caused by an imbalance in blood flow in the placental vasculature such that one twin becomes overperfused (recipient) and its co-twin is underperfused (donor). It complicates up to 15% of all monochorionic twins.

The twin peak sign (also called lambda sign) is a triangular projection of tissue with the same echogenicity as the placenta, extending beyond the chorionic surface of the placenta. Its presence is pathognomonic of dichorionicity, however, it cannot be consistently identified in later gestation. The other feature that rules out monochorionicity is the identification of different genders of the twins. Membrane thickness is also sometimes used to determine chorionicity. However, depending on the gestational age at evaluation, membrane thickness alone can be unreliable to distinguish between dichorionic (thick membrane greater than 2 mm) and monochorionic (thin layer) placentas.

Prenatal diagnosis of twin–twin transfusion syndrome requires a high level of suspicion. The syndrome usually is characterized by certain ultrasonographic findings (Box 85-1). Not all the ultrasonographic findings are required in order to make a diagnosis of twin–twin transfusion syndrome and none are specific to it.

Categorization of the severity of twin–twin transfusion syndrome is commonly done with the Quintero staging system (Table 85-1). In severe cases, the donor twin shows growth restriction, decreased amniotic fluid volume, absence of visualization of fetal bladder, and abnormal umbilical artery Doppler studies, whereas the recipient twin shows signs of fluid overload, including increased amniotic fluid volume and hydrops fetalis. Once a diagnosis of twin–twin transfusion syndrome has been made, close surveillance is required because not all cases show an orderly progression through the stages (I–V) before development of perinatal complications. Depending on the clinical circumstances both amnioreduction and laser photo coagulation may be used for treatment of advanced cases.

In the described case, the presence of a twin peak sign on ultrasonography would essentially rule out twin–twin

BOX 85-1

Ultrasonographic Features of Twin–Twin Transfusion Syndrome

- Presence of single placenta
- Gender concordance
- Significance growth discordance (usually greater than 20%)
- Discrepancy in amniotic fluid volume
- Thin membrane and absence of twin peak sign
- Presence of fetal hydrops or cardiac dysfunction
- Abnormal umbilical artery Doppler findings, such as absent end diastolic flow in donor fetus

Taylor MJ, Govender L, Jolly M, Wee L, Fisk NM. Validation of the Quintero staging system for twin–twin transfusion syndrome. Obstet Gynecol 2002;100:1257–65.

TABLE 85-1. Quintero Staging System for Twin–Twin Transfusion Syndrome

Stage	Findings
Stage I	The fetal bladder of the donor twin remains visible, fetal Doppler values normal
Stage II	The bladder of the donor twin is collapsed and not visible, fetal Doppler values normal
Stage III	The bladder of the donor twin is collapsed and not visible, fetal Doppler values critically abnormal
Stage IV	Fetal hydrops present
Stage V	Demise of either twin

Modified from Taylor MJ, Govender L, Jolly M, Wee L, Fisk NM. Validation of the Quintero staging system for twin–twin transfusion syndrome. Obstet Gynecol 2002;100:1257–65.

transfusion syndrome because the twin peak sign is indicative of dichorionicity. Twin–twin transfusion syndrome is not characterized by the presence of a renal abnormality, but instead by the presence of oligohydramnios in one sac and polyhydramnios in the other sac.

Baschat A, Chmait RH, Deprest J, Gratacós E, Hecher K. Twin-to-twin transfusion syndrome (TTTS). WAPM Consensus Group on Twin-to-Twin Transfusion. J Perinat Med 2011;39:107–12.

Roberts D, Gates S, Kilby M, Neilson JP. Interventions for twin–twin transfusion syndrome: a Cochrane review. Ultrasound Obstet Gynecol 2008;31:701–11.

Taylor MJ, Govender L, Jolly M, Wee L, Fisk NM. Validation of the Quintero staging system for twin–twin transfusion syndrome. Obstet Gynecol 2002;100:1257–65.

Thorson HL, Ramaeker DM, Emery SP. Optimal interval for ultrasound surveillance in monochorionic twin gestations. Obstet Gynecol 2011;117:131–5.

86

Appendicitis in pregnancy

A 32-year-old woman, gravida 3, para 2, at 33 weeks of gestation comes to your hospital's emergency department for evaluation of abdominal pain. She has had episodic abdominal, back, and flank pain for 2 days, associated with malaise, nausea, and vomiting. She has noticed increased uterine cramping and contractions. Her temperature is 38.2°C (100.8°F). She is normotensive with a pulse of 110 beats per minute, and a respiratory rate of 20 breaths per minute. She appears uncomfortable but is in no acute distress. She is slightly diaphoretic with a normal cardiopulmonary examination. Her abdomen is gravid, with pronounced tenderness in the lower quadrants and right flank. Cervical examination shows a 1-cm cervix, 20% effaced, and the presenting part is ballotable. The fetal heart rate is 160 beats per minute and reassuring. Uterine monitoring shows irregular contractions. Laboratory evaluation reveals a white blood cell count of 16.3×10^9/L with an increase in neutrophils and a hematocrit of 33%. The urinalysis is notable for trace blood and leukocyte esterase. The most appropriate next diagnostic test is

(A) amniocentesis
(B) computed tomography (CT)
(C) magnetic resonance imaging (MRI)
* (D) ultrasonography

The two most common conditions associated with an acute gravid abdomen are appendicitis and cholecystitis. In order to avoid missing the diagnosis of acute appendicitis, a high degree of clinical suspicion must be maintained. The prevalence of disease is similar in pregnant and nonpregnant women. The risk of perforation, up to 40%, is higher in pregnant women. One reason for the increased rupture rate may be an understandable reluctance to operate on a pregnant patient suspected to have appendicitis. The classic symptoms of acute appendicitis include fever, nausea, vomiting, anorexia, and right lower quadrant pain. Changes in intra-abdominal anatomic relationships in pregnancy also may complicate examination and imaging findings. Without a timely diagnosis, appendiceal perforation and subsequent peritonitis increase morbidity and mortality, including preterm delivery. One of the most common nonobstetric surgical procedures performed on pregnant patients is appendectomy.

The diagnosis of appendicitis in pregnancy begins clinically. If the diagnosis is unclear, additional evidence must be sought in a timely manner. Because ultrasonography is widely available, does not involve radiation exposure, and has an excellent safety profile, it should be considered the first choice in imaging patients with suspected appendicitis. However, operator-specific performance may affect detection. The appropriate technique is compression graded ultrasonography, in which a diagnostic result is a noncompressible tubular structure in the right lower quadrant with a diameter greater than 6 mm. The sensitivity of ultrasonography in diagnosing appendicitis in pregnancy ranges from 48% to 100%, the specificity from 96% to 100%, and the accuracy, or percentage of correct test results, from 50% to 98%. In cases where ultrasonography demonstrates a positive result, the patient should proceed to appendectomy.

Combined with the possibility of nondiagnostic testing, as high as 70% in pregnancy, these performance characteristics do not offer sufficient reassurance for health care providers to stop at ultrasonography alone if the test is nondiagnostic. In cases with a high degree of clinical suspicion but with nondiagnostic ultrasonography, CT or MRI scan should be obtained next. A systematic review did not identify a significant performance difference between the two modalities. Selection should be based on availability and time constraints first, because a delay in diagnosis causing perforation may double the rate of miscarriage or infant mortality. If both modalities are immediately available, MRI may be preferred to avoid ionizing radiation exposure and because contrast administration may be easier. Paramagnetic contrast agents (such as gadolinium) used in MRI have not been studied sufficiently in pregnancy but are unlikely to cause harm; as with ionizing radiation, their use should be justified by the potential benefit to the patient. The ionizing radiation exposure from one abdominal CT scan is below the acceptable threshold for fetal risk and should not be considered a contraindication if the test is indicated.

In this case, the presence of significant abdominal tenderness strongly suggests appendicitis. In patients who do not have such pronounced localizing symptoms, other diagnoses should be considered. Amniocentesis may be a helpful adjunct in cases where abdominal tenderness in

pregnancy is not accompanied by other classic findings of intraamniotic infection. Amniotic fluid studies, such as Gram stain, culture, and glucose levels, may identify early amnionitis.

If the decision to perform surgery has been made, the appendix must be removed regardless of appearance, because the definitive diagnosis is made histologically. Laparoscopic appendectomy is feasible in all trimesters, but the risks compared with open appendectomy are still not clearly understood.

Basaran A, Basaran M. Diagnosis of acute appendicitis during pregnancy: a systematic review. Obstet Gynecol Surv 2009;64:481,8; quiz 499.

Gilo NB, Amini D, Landy HJ. Appendicitis and cholecystitis in pregnancy. Clin Obstet Gynecol 2009;52:586–96.

Guidelines for diagnostic imaging during pregnancy. ACOG Committee Opinion No. 299. American College of Obstetricians and Gynecologists. Obstet Gynecol 2004;104:647–51.

McGory ML, Zingmond DS, Tillou A, Hiatt JR, Ko CY, Cryer HM. Negative appendectomy in pregnant women is associated with a substantial risk of fetal loss. J Am Coll Surg 2007;205:534–40.

87

Smoking cessation

A patient visits you for preconception counseling. She is healthy with no remarkable medical history. She smokes a pack of cigarettes a day. She has tried to quit many times but has been unsuccessful. She has been taking varenicline for 1 month as prescribed by her family physician. She is taking no other medication. She reports frequent crying episodes and difficulty getting out of bed. When depressive symptoms occur in a patient who is taking varenicline, the best next step in management is

(A) offer the patient supportive care
* (B) discontinue varenicline
(C) add a selective serotonin reuptake inhibitor
(D) decrease the dose of varenicline

Smoking during pregnancy is associated with many adverse pregnancy outcomes such as intrauterine growth restriction, placental abruption, and preterm delivery. Approximately 5–8% of preterm deliveries and 13–19% of term infants with low birth weight can be attributed to smoking. After birth, newborns continue to be at risk for colic and sudden infant death syndrome. Smoking is a modifiable risk factor that if stopped can improve pregnancy outcomes. Almost one half of women stop smoking immediately before or during pregnancy. Therefore, this patient is likely highly motivated to quit.

Health care providers can play a valuable role in encouraging patients to quit smoking by advising them about the five A's of smoking cessation (Box 87-1). Counseling alone or with self-help materials increases smoking cessation rates. Counseling alone is effective in 20% of patients. In addition to counseling, the patient also can be provided with the Internet addresses of helpful web sites to enable her to gain access to information on smoking cessation provided by various organizations (Box 87-2).

Pharmacotherapy is an alternative for patients who cannot quit with counseling alone. Several medications have been approved by the U.S. Food and Drug Administration (FDA) as aids for smoking cessation:

- Sustained-release bupropion (also known as bupropion SR)
- Nicotine gum
- Nicotine inhaler
- Nicotine nasal spray
- Nicotine patch
- Varenicline

Bupropion SR is an antidepressant that weakly inhibits the neuronal uptake of dopamine, norepinephrine, and serotonin. Nicotine gum, inhaler, nasal spray, and patch are nicotine replacement products. Varenicline binds to the neuronal nicotinic acetylcholine receptor and acts as a nicotine antagonist as well as a partial agonist. No well studied or accepted algorithm has been devised to guide the optimal selection of medication. During pregnancy, bupropion SR and varenicline are classified by the FDA as category C, whereas nicotine replacement is classified as category D. The major concern with nicotine replace-

BOX 87-1

The Five A's of Smoking Cessation

- *Ask* about cigarette use during preconception counseling and at the first prenatal visit.
- *Advise* the patient of the risks to her and to her fetus.
- *Assess* the patient's willingness to stop smoking.
- *Assist* the patient who desires to quit.
- *Arrange* follow-up to track the patient's progress.

Adapted from Smoking cessation during pregnancy. Committee Opinion No. 471. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010; 116:1241–4.

BOX 87-2

Web Site Resources for Smoking Cessation in Pregnant Patients

Name of Organization	Web Address
American Cancer Society	http://www.cancer.org
American Heart Association	http://www.heart.org/HEARTORG/
National Cancer Institute	http://www.cancer.gov
National Partnership to Help Pregnant Smokers Quit	http://www.helppregnantsmokersquit.org/quit/
Smokefree.gov	http://www.smokefree.gov/

ment is that it may have some of the same adverse events as smoking.

Varenicline was approved for sale in the United States in 2006. Varenicline provides withdrawal relief through its partial agonist effect, which inhibits the reinforcing effects of nicotine. Common adverse effects of the medication are constipation, flatulence, nausea, vomiting, dream disorder, headache, insomnia, and sleep disorder. In the postmarketing experience, serious neuropsychiatric adverse effects, such as depression, suicidal ideation, attempted suicide, and completed suicide, have been reported. As a result, the FDA issued a black box warning that patients being treated with varenicline should be observed for changes in behavior, hostility, agitation, depressed mood, and suicidal ideation.

If a patient develops such symptoms, varenicline should be discontinued immediately instead of adjusting the dose. After the medication is stopped, ongoing monitoring and supportive care is advised. If the symptoms persist, the patient may need professional counseling or medication, such as a selective serotonin reuptake inhibitor, for the treatment of depression. Varenicline should be used with caution in a patient with a preexisting psychiatric illness. Before initiating therapy, the risks of varenicline should be weighed against the benefits of its use. Based on the relative paucity of information on pharmacologic methods of smoking cessation in pregnancy, the use of such treatment should be considered only after nonpharmacologic methods of smoking cessation have failed.

Fiore MC, Jaen CR, Baker TB, Bailey WC, Benowitz NL, Curry SJ, et al. Treating tobacco use and dependence: 2008 update. Clinical Practice Guideline. Rockville (MD): U.S. Department of Health and Human Services; 2008. Available at: http://www.surgeongeneral.gov/tobacco/treating_tobacco_use08.pdf. Retrieved November 7, 2011.

Forest S. Controversy and evidence about nicotine replacement therapy in pregnancy. MCN Am J Matern Child Nurs 2010;35:89–95.

Mundey K. An appraisal of smoking cessation aids. Curr Opin Pulm Med 2009;15:105–12.

Murthy P, Subodh BN. Current developments in behavioral interventions for tobacco cessation. Curr Opin Psychiatry 2010;23:151–6.

Smoking cessation during pregnancy. Committee Opinion No. 471. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:1241–4.

Varenicline. Micromedex Healthcare Series [Internet database]. Greenwood Village, CO: Thomson Micromedex. Updated periodically.

88

Pyelonephritis

A woman at 19 weeks of gestation visits your office. She has had general malaise for several days with nausea and vomiting, right side back pain, fever, and chills. Physical examination reveals a temperature of 39.5°C (103°F), respiratory rate of 16 breaths per minute, pulse of 115 beats per minute, and blood pressure of 120/80 mm Hg. She demonstrates costovertebral angle (CVA) tenderness and a normal abdominal examination. She has good capillary refill. Her uterus is at the umbilicus and nontender. The fetal heart rate is 180 beats per minute. Her complete blood count reveals a white blood count of 16,000/mm^3. Microscopic urinalysis shows many white blood cells and bacteria per high power field. The most likely diagnosis is

(A) appendicitis
(B) cystitis
(C) sepsis
(D) chorioamnionitis
* (E) pyelonephritis

Urinary tract infections are characterized as either lower or upper tract infections. Lower tract infections include asymptomatic bacteriuria and cystitis, whereas pyelonephritis is classified as an upper tract infection. The incidence of asymptomatic bacteriuria is 5–6% in women and is found equally in pregnant and nonpregnant women. Although treatment of asymptomatic bacteriuria is not recommended in nonpregnant patients, treatment is recommended in pregnant patients. If women with asymptomatic bacteriuria are left untreated during their pregnancy, 25% of these women will develop pyelonephritis. Most physicians use 100,000 cfu/mL of a single pathogen on a clean catch urine culture to diagnose asymptomatic bacteriuria. The most common cause of asymptomatic bacteriuria is normal perineal flora.

A patient with cystitis presents with dysuria, frequency, urgency, or a mixture of these three symptoms. Unlike patients with pyelonephritis, a patient with cystitis does not usually have any systemic complaints. The diagnosis is suspected if the patient has either leukocyte esterase or nitrites in her urine and is confirmed by culture.

Pyelonephritis typically occurs in the second trimester and third trimester but can occur in the first trimester, especially in individuals with diabetes mellitus. As in this patient, the associated symptoms are flank pain, fever, nausea, and vomiting. The patient may not have any symptoms of lower genital tract infection. On physical examination, costovertebral angle tenderness is present much more commonly on the right side rather than on the left side or on both sides. Because of the association between adverse pregnancy outcome and pyelonephritis, pregnant patients usually are treated as hospital inpatients with intravenous antibiotics.

Up to 20% of patients with pyelonephritis can develop sepsis. The hallmark of sepsis is a microbial infection with a systemic inflammatory response (such as hyperthermia or hypothermia, tachycardia, tachypnea, or hypotension), and evidence of end organ dysfunction, hypoxia, or increased serum lactate. In the described patient, end organ dysfunction is not evident although careful monitoring for progression to sepsis should be carried out. Patients with sepsis can experience serious complications, such as respiratory distress with or without adult respiratory distress syndrome, renal failure, disseminated intravascular coagulopathy, and septic shock.

Appendicitis is the most common nonobstetric cause of acute abdomen in pregnancy. The diagnosis is challenging during pregnancy because many of the signs and symptoms are blunted or atypical. Appendicitis usually presents as colicky epigastric or periumbilical pain that eventually localizes to the right side. However, the appendix is displaced upwardly starting at 12 weeks of gestation, so the right-sided pain may not be in the same location as in the nonpregnant patient. In most cases, a fever is not present. Graded compression ultrasonography may be helpful in diagnosing acute appendicitis. If the appendix is not visible on ultrasonography, additional imaging may be warranted.

Chorioamnionitis usually occurs in women in labor with prolonged or preterm rupture of membranes. The clinical diagnosis of chorioamnionitis is imprecise and can be difficult to make especially during labor. The classic definition is a fever of 38°C (100.4°F) and at least two other findings: maternal or fetal tachycardia or both, maternal leukocytosis, uterine tenderness, and foul-smelling amniotic fluid.

Ovalle A, Levancini M. Urinary tract infections in pregnancy. Curr Opin Urol 2001;11:55–9.

Sharp HT. The acute abdomen during pregnancy. Clin Obstet Gynecol 2002;45:405–13.

Sheffield JS, Cunningham FG. Urinary tract infection in women. Obstet Gynecol 2005;106:1085–92.

Treatment of urinary tract infections in nonpregnant women. ACOG Practice Bulletin No. 91. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008;111:785–94.

van Dillen J, Zwart J, Schutte J, van Roosmalen J. Maternal sepsis: epidemiology, etiology and outcome. Curr Opin Infect Dis 2010;23: 249–54.

89

Multiple sclerosis

A 34-year-old woman with a history of relapsing and remitting multiple sclerosis sees you for a preconception consultation. She asks about the chance of having a relapse during pregnancy. You inform her that her chance of relapse is highest during the

(A) first trimester
(B) second trimester
(C) third trimester
* (D) postpartum period

Multiple sclerosis is a chronic inflammatory disease of the central nervous system. After trauma, multiple sclerosis is the leading cause of neurologic disability in young adults. Onset usually occurs during the reproductive years, between ages 20 years and 40 years, and two thirds of cases are observed in women. In the United States, there is a geographic disparity in prevalence. In the northern states, the prevalence is 200 per 100,000, whereas in the southern half of the country, it is less than 50 per 100,000. Multiple sclerosis is more common in persons of northern European descent compared with persons of African, Asian, and Hispanic descent.

Multiple sclerosis can affect the brain, spinal cord, and optic nerves. Demyelination and axonal damage, caused by proinflammatory immune dysregulation, acts to disrupt nerve transmission causing the signs and symptoms of multiple sclerosis. Symptoms include sensory loss (numbness, tingling, or burning pain); muscle weakness, spasticity or fatigability; visual loss or scotomata; diplopia, ataxia, and bladder dysfunction. Unexplained unusual fatigue is also a very common symptom.

Multiple sclerosis is typically divided into two categories: relapsing–remitting and progressive. Approximately 85% of patients have the relapsing–remitting type of the disease characterized by neurologic symptoms that last longer than 24 hours and typically persist for days or weeks, followed by slow improvement or stabilization. These patients will experience times without escalating symptoms. However, there may be incomplete recovery from a relapse and disability can increase over time. In primary progressive multiple sclerosis, there is a gradual decline in function from the onset. These patients do not have periods of quiescence or distinct flares.

Pregnant women with multiple sclerosis are concerned about the effect of their illness on their pregnancy and vice versa. In the past, it was felt that pregnancy increased the risk of relapse and worsened the course of the disease. Several studies have shown that this not the case. Pregnancy seems to be associated with a temporary beneficial immune state for patients with multiple sclerosis partially mediated through an effect on T lymphocyte subsets.

A large prospective study of multiple sclerosis patients who had full-term pregnancies reported a reduction in relapse during pregnancy that was most pronounced in the third trimester. The risk of relapse increased during the first 3 months postpartum then returned to its prepregnancy rate by 6 months postpartum. Some predictors of postpartum relapse include a high rate of relapse in the prepregnancy year and during the current pregnancy, and a high level of disability at the time of pregnancy. Breastfeeding women may have a lower rate of relapse than women who do not breastfeed. However, this reported effect may be the result of the selection bias as women who choose to breastfeed have fewer relapses and lower disability scores. Overall, the rate of relapse during the "pregnancy year" (ie, 9 months of pregnancy and 3 months postpartum) is similar to the rate of relapse before pregnancy. In regard to advice for the described patient, she should be counseled that her chance of relapse is highest during the postpartum period.

Confavreux C, Hutchinson M, Hours MM, Cortinovis-Tourniaire P, Moreau T. Rate of pregnancy-related relapse in multiple sclerosis. Pregnancy in Multiple Sclerosis Group. N Engl J Med 1998;339:285–91.

Lee M, O'Brien P. Pregnancy and multiple sclerosis. J Neurol Neurosurg Psychiatry 2008;79:1308–11.

Vukusic S, Hutchinson M, Hours M, Moreau T, Cortinovis-Tourniaire P, Adeleine P, et al. Pregnancy and multiple sclerosis (the PRIMS study): clinical predictors of post-partum relapse. The Pregnancy in Multiple Sclerosis Group; Pregnancy in Multiple Sclerosis Group [published erratum appears in Brain 2004;127:1912]. Brain 2004;127:1353–60.

Waubant E, Crabtree-Hartman E. Multiple sclerosis. Clin Update Womens Health Care 2010;IX(5):1–76

90

Mitral valve prolapse and subacute bacterial endocarditis

A 26-year-old primigravid woman at 30 weeks of gestation presents with palpitations. Electrocardiogram and thyroid-stimulating hormone level are normal. Maternal echocardiogram demonstrates mitral valve prolapse with mild mitral regurgitation. She has no other cardiac abnormalities. She has a history of rash with penicillin use. Based on current American Heart Association recommendations for subacute bacterial endocarditis prophylaxis, at delivery she should be prescribed

(A) ampicillin
(B) cefazolin
(C) clindamycin
(D) vancomycin and gentamicin
* (E) no antibiotic prophylaxis

Mitral valve prolapse is the most common cardiac valve abnormality; it occurs in approximately 6% of the female population. The posterior leaflet of the mitral valve prolapses into the left atrium, sometimes allowing retrograde leakage of blood into the left atrium during systole. It may occur with or without regurgitation and usually is considered a benign condition, although it may contribute to atrial fibrillation, heart failure, and stroke. Symptoms associated with mitral valve prolapse include dyspnea, fatigue, anxiety, palpitations, and chest pain. Although nonspecific electrocardiographic changes can be seen, echocardiography is the standard mode of diagnosis.

Mitral valve prolapse and mitral regurgitation are considered to be lesions of low risk for subacute bacterial endocarditis. In 2007, the American Heart Association revised its guidelines for the prevention of subacute bacterial endocarditis, specifying that only the highest-risk cardiac lesions should be considered for prophylaxis (Box 90-1). Even with a high-risk lesion, prophylaxis is not recommended for uncomplicated vaginal or cesarean deliveries. In fact, normal delivery is associated with a less than 5% risk for bacteremia. Thus, type of lesion is not significant in choosing endocarditis prophylaxis for routine cases of delivery. However, in cases where the risk for bacteremia may be increased, such as patients with chorioamnionitis, pyelonephritis, or endometritis, a regimen effective for bacterial endocarditis should be selected, and intravenous administration should be used (Table 90-1).

Women with high-risk cardiac lesions (Box 90-1) should receive prophylaxis for dental procedures that include disruption or manipulation of the gingival tissue. For these cases, oral administration is appropriate for patients without penicillin allergies. Anesthesia, general cleaning, cavity filling, or placing or adjusting orthodontic devices are dental procedures that do not require prophylaxis.

Use of prophylactic antibiotics in labor and delivery. Practice Bulletin No. 120. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:1472–83.

BOX 90-1

Cardiac Conditions With High Risk of Endocarditis in the Presence of Bacteremia

Prophylaxis against infective endocarditis is reasonable for the following patients at highest risk of adverse outcomes from infective endocarditis who undergo dental procedures that involve manipulation of either gingival tissue or the periapical region of teeth or perforation of the oral mucosa*:

- Patients with prosthetic cardiac valve or prosthetic material used for cardiac valve repair
- Patients with previous infective endocarditis
- Patients with CHD
  - — Unrepaired cyanotic CHD, including palliative shunts and conduits
  - — Completely repaired congenital heart defect repaired with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure.
  - — Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (both of which inhibit endothelialization)
- Cardiac transplant recipients with valve regurgitation due to a structurally abnormal valve.

Abbreviation: CHD, congenital heart disease.

*Prophylaxis against infective endocarditis is not recommended for nondental procedures in the absence of active infection.

Data from Nishimura RA, Carabello BA, Faxon DP, et al. ACC/AHA 2008 guideline update on valvular heart disease: focused update on infective endocarditis. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: endorsed by the Society of Cardiovascular Anesthesiologists, Society of Cardiovascular Angiography, and Society of Thoracic Surgeons. Circulation 2008;118:887–96.

Use of prophylactic antibiotics in labor and delivery. Practice Bulletin No. 120. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:1472–83.

TABLE 90-1. Antibiotic Prophylaxis Appropriate for Infective Endocarditis

Treatment	Antibiotic	Regimen (Preferable Treatment of Antibiotic 30–60 Minutes Before Procedure)
Intravenous therapy	Ampicillin	2 g intravenously
	or	
	Cefazolin or ceftriaxone*	1 g intravenously
Allergic to penicillin or ampicillin†	Cefaxolin or ceftriaxone*	1 g intravenously*
	or	
	Clindamycin†	600 mg intravenously*
Oral	Amoxicillin	2 g

*This regimen does not cover enterococcus. Vancomycin can be used if enterococcus is of concern.

†Cephalosporins should not be used in patients with a significant sensitivity to penicillin.

Use of prophylactic antibiotics in labor and delivery. Practice Bulletin No. 120. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:1472–83.

91

Monochorionic twins

A 26-year-old woman, gravida 2, para 1, visits you for prenatal care at 9 weeks of gestation estimated by her last menstrual period. You perform ultrasonography, which demonstrates a twin pregnancy, with a dividing membrane between both fetuses, consistent with menstrual dating. At this gestational age, the most sensitive and specific ultrasonographic sign to diagnose a monochorionic pregnancy is

(A) number of yolk sacs
* (B) "T" sign at the membrane insertion
(C) fetal sex determination
(D) a single placenta

Determination of chorionicity is an important first step in the management of twin pregnancies. Although the frequency varies across specific populations, in general, monochorionic pregnancies account for up to 20% of all twin pregnancies, including twin pregnancies that arise from in vitro fertilization. Monochorionic twins are associated with a threefold to fivefold increased risk of morbidity compared with dizygotic twins. Counseling and surveillance is particularly important given the 5–15% risk of twin–twin transfusion syndrome in monochorionic twins.

Chorionicity is best assessed by ultrasonography in the first trimester or early second trimester. Discordant sex is a highly sensitive sign for diagnosing a dichorionic pregnancy, but this can only be done starting in the second trimester. Observing two separate placentas is the next most sensitive (greater than 97%) and specific (100%) sign for the diagnosis of dichorionicity.

The absence of these signs (ie, cases of sex concordance or when there is a single placental mass) is not a specific indicator of monochorionicity and, therefore, other sonographic features must be evaluated. In these cases, observation of the "T" sign where the inter-twin membrane inserts into the placenta has 100% sensitivity and greater than 98% specificity for predicting monochorionic twins (Fig. 91-1). Presence of the "lambda" or "twin peak" sign is likewise highly diagnostic for dichorionic twins (Fig. 91-2).

Thickness of the intertwin membrane has been proposed as an additional technique. Four layers of membranes (two amnions, two chorions) comprise the intertwin membrane for dichorionic pregnancies, as opposed to two layers (two amnions) in monochorionic twins. Thus, the mean membrane thickness is larger in dichorionic than monochorionic pregnancies (2.4 mm versus 1.4 mm). Although improvements in ultrasound technology have made this measurement easier, a lack of consensus on the appropriate cutoff measurement and the substantial interobserver and intraobserver variability limit its clinical utility.

Number of yolk sacs alone is a poor determinant of amnionicity or chorionicity. Most monochorionic preg-

FIG. 91-1. T-sign, highly diagnostic for predicting monochorionic twins. (Courtesy of Christian M. Pettker, MD, Yale University School of Medicine.)

FIG. 91-2. Lambda or twin peak sign, highly diagnostic for dichorionic twins. (Courtesy of Christian M. Pettker, MD, Yale University School of Medicine.)

nancies will have two yolk sacs, although the presence of two embryos and a single yolk sac may indicate a monoamniotic gestation.

Bromley B, Benacerraf B. Using the number of yolk sacs to determine amnionicity in early first trimester monochorionic twins. J Ultrasound Med 1995;14:415–9.

Lee YM, Cleary-Goldman J, Thaker HM, Simpson LL. Antenatal sonographic prediction of twin chorionicity. Am J Obstet Gynecol 2006;195:863–7.

Multiple gestation: complicated twin, triplet, and high-order multifetal pregnancy. ACOG Practice Bulletin No. 56. American College of Obstetricians and Gynecologists. Obstet Gynecol 2004;104:869–83.

Shetty A, Smith AP. The sonographic diagnosis of chorionicity. Prenat Diagn 2005;25:735–9.

Wan JJ, Schrimmer D, Tache V, Quinn K, Lacoursiere DY, James G, et al. Current practices in determining amnionicity and chorionicity in multiple gestations. Prenat Diagn 2011;31:125–30.

92

Shoulder dystocia

A 31-year-old woman, gravida 2, para 1, comes to the labor unit in active labor at 37 weeks of gestation. She progresses normally through labor and delivers the fetal head, which retracts back against the perineum. Downward traction does not produce any further progress. The nurses position the patient with her legs hyperflexed and abducted and provide suprapubic pressure. If delivery does not occur, the next step should be

(A) additional traction
(B) cesarean delivery
(C) lateral head displacement
* (D) posterior arm delivery
(E) proctoepisiotomy

Shoulder dystocia is an unpredictable obstetric emergency that results primarily from impaction of the anterior shoulder behind the maternal pubic symphysis. It occurs in approximately 0.19–3.0% of pregnancies, most often in normal-weight infants. Risk factors for shoulder dystocia include fetal macrosomia, maternal diabetes mellitus, maternal obesity, instrumental delivery, and postterm pregnancy, but prospective trials have demonstrated that these risk factors perform poorly as predictors of shoulder dystocia. Potential complications of shoulder dystocia include increased risk of clavicular fracture, brachial plexus injury, depressed 5-minute Apgar scores, and increased admission rates to intensive care nurseries. Most cases of shoulder dystocia are resolved without maternal or neonatal injury. Because shoulder dystocia is rare, unpredictable, and requires urgent intervention, it is extremely difficult to study in large prospective trials that might answer questions regarding the most effective intervention.

Shoulder dystocia management relies on altering the geometry of the fetus in relation to the maternal pelvis in order to permit continued progress of the arrested shoulder, in most cases the anterior shoulder, through the pelvis. Additional traction without changing the geometry is unlikely to help and may increase the risk of injury to the brachial plexus. For the same reason, the mother should be advised to stop pushing when a dystocia is identified.

The initial recommended maneuvers manipulate the parturient. The McRoberts maneuver is performed by flexing the maternal thighs onto the abdomen in a supine position. The angle between the sacrum and lumbar spine is lessened, rotating the pubic symphysis cephalad and anterior, allowing the posterior shoulder to descend further into the sacral curve resulting in release of the anterior shoulder. A similar effect can be accomplished by positioning the mother on all fours (Gaskin maneuver), which in one study required only 2–3 minutes and did not result in brachial plexus injury when used as the primary management technique. Suprapubic pressure, directed posteriorly or at an angle, may dislodge the affected shoulder by rotating the shoulder girdle into an oblique axis.

The subsequent group of maneuvers requires manipulation of the fetus. Rotational maneuvers, such as the Woods or Rubin maneuvers, use pressure applied directly to the fetal shoulder in an attempt to turn the shoulder girdle to an oblique position. Delivery of the posterior arm

can reduce the working diameter of the shoulder girdle by 20% and facilitate delivery. Care should be used in delivery of the posterior arm to avoid humeral fracture.

In a large retrospective cohort study that examined outcomes of maneuvers for relieving shoulder dystocia, the maneuver with the highest rate of success was delivery of the posterior shoulder at 84.4%. In descending order, the other maneuvers and their success rates were the Woods corkscrew (72.0%), Rubin maneuver (66.0%), supra-pubic pressure (62.2%), and McRoberts maneuver (24.3%). The Gaskin maneuver (all-fours positioning), Zavanelli maneuver (head replacement), and fundal pressure were not evaluated because of low rates of use. When used as a secondary maneuver after McRoberts maneuver and suprapubic pressure, delivery of the posterior arm was the only method not associated with fetal injury when cases were adjusted for parity, maternal age, race, site of care, and birth weight. For these reasons, posterior arm delivery is the best step to try next in the described case.

Proctoepisiotomy will not directly resolve a dystocia, because the problem is not one of soft tissues, but can create more space for direct manipulation of the fetus if access is difficult. Use of proctoepisiotomy is associated with a sevenfold increase in perineal trauma without reducing brachial plexus injury or neonatal depression. Lateral displacement of the fetal head (relative to the fetal spine, not the maternal) increases the potential stretching distance of the brachial plexus and should be avoided.

Drastic maneuvers, such as cephalic replacement (the Zavanelli maneuver), symphysiotomy, or hysterotomy, are reserved for cases where repeated attempts at the previous maneuvers have failed to achieve delivery. Although the reported success rate for the Zavanelli maneuver is high, approximately 90–92%, it is associated with serious fetal and maternal injuries. In the described patient, cesarean delivery would require performance of the Zavanelli maneuver first, and would not be recommended before less aggressive maneuvers are attempted.

Athukorala C, Middleton P, Crowther CA. Intrapartum interventions for preventing shoulder dystocia. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD005543. DOI: 10.1002/14651858.CD005543.pub2.

Gherman RB, Chauhan S, Ouzounian JG, Lerner H, Gonik B, Goodwin TM. Shoulder dystocia: the unpreventable obstetric emergency with empiric management guidelines. Am J Obstet Gynecol 2006;195:657–72.

Hoffman MK, Bailit JL, Branch DW, Burkman RT, Van Veldhusien P, Lu L, et al. A comparison of obstetric maneuvers for the acute management of shoulder dystocia. Obstet Gynecol 2011;117:1272–8.

Shoulder dystocia. ACOG Practice Bulletin No. 40. American College of Obstetricians and Gynecologists. Obstet Gynecol 2002;100:1045–50.

93

Alcohol use in pregnancy

A 24-year-old Hispanic woman reports alcohol use during pregnancy. She is a college graduate and works for a nonprofit agency making approximately $45,000 a year. The demographic factor most associated with her use of alcohol in pregnancy is

(A) age
(B) income
(C) ethnicity
* (D) education

Alcohol use in pregnancy is considered a leading cause of preventable birth defects and developmental disability in the United States. Fetal alcohol syndrome (FAS) is reported to occur in between 0.5 and 2 per 1,000 live-births. The Centers for Disease Control and Prevention diagnostic criteria for FAS require all three of the following:

1. Facial abnormalities: smooth philtrum, thin vermillion border, and small palpebral fissures (all required)
2. Growth deficit: prenatal or postnatal
3. Central nervous system abnormalities: structural, neurologic, or functional

Consensus exists that alcohol exposure during pregnancy may lead to a range of effects that do not fulfill the criteria for FAS. These disorders have been called fetal alcohol spectrum disorders (FASDs). At this time, there are no specific diagnostic criteria for FASDs; however, it is estimated that cases of FASD are at least three times more frequent than cases of FAS.

Alcohol use among pregnant women is very prevalent. In a national survey on alcohol use during pregnancy, data for 2006–2007 showed that 11.8% of pregnant women used alcohol in the past month. The rate of women who used alcohol in the past month had not decreased when compared with data from 2002 to 2003. There is variation in the demographic characteristics of women who report alcohol use in pregnancy (Table 93-1). When considering age, the lowest prevalence of reported use in pregnancy is among 18–25-year-old women. Hispanic women report a three to four times lower use in pregnancy compared with non-Hispanic white women and black women. Alcohol use in pregnancy increases with increasing educational attainment. College graduates have the highest reported use at 15.8%. Both low income and high income pregnant women have increased prevalence of use compared with middle income women. Women with incomes of $75,000 or higher have the highest percentage of alcohol use. Although clinicians should be aware of demographic risk factors, they can not be used for selective screening for alcohol use because even in lower risk groups alcohol use is prevalent. Universal screening is recommended with a tool, such as the T-ACE questionnaire (Table 93-2).

TABLE 93-1. Percentage of Past Month Alcohol Use Among Pregnant Women Aged 15–44 Years by Demographic Characteristics, 2006–2007

Demographic Characteristic	% Use
Age (years)	
15–17	15.8
18–25	9.8
26–44	12.5
Race/ethnicity	
White	14.5
Black	15.7
Hispanic	4.1
Educational status	
Less than high school	8.9
High school graduate	8.3
Some college	11.7
College graduate	15.8
Income	
Less than $20,000	11.7
$20,000 to $49,999	9.2
$50,000 to $74,999	9.5
$75,000 or higher	16.3

Substance Abuse and Mental Health Services Administration, Office of Applied Studies. The NSDUH Report: Alcohol Use among Pregnant Women and Recent Mothers: 2002 to 2007. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2008. Available at http://www.samhsa.gov/data/2k8/pregnantAlc/pregnantAlc.htm. Accessed January 30, 2012.

There is no level of alcohol exposure in pregnancy that is considered "safe." All women should be advised to abstain from alcohol during pregnancy. The American College of Obstetricians and Gynecologists has published an interventional tool kit to help clinicians prevent FAS

TABLE 93-2. The T-ACE Problem Drinking Screen

Code	Factor	Cut-Points	Score	Question
"T"	Tolerance	≥2 or ≥3 drinks	2	How many drinks does it take to make you feel high?
"A"	Annoy	Yes/No	1	Has anybody ever annoyed you by complaining about your drinking?
"C"	Cut Down	Yes/No	1	Have you ever felt you ought to cut down on your drinking?
"E"	"Eye-Opener"	Yes/No	1	Have you ever needed a drink first thing in the morning to get going?

Total T-ACE Score Cut-Points: 2 or 3.

Chiodo LM, Sokol RJ, Delaney-Black V, Janisse J, Hannigan JH. Validity of the T-ACE in pregnancy in predicting child outcome and risk drinking. Alcohol 2010;44:595–603. Copyright 2010 by Elsevier.

and FASDs. It is available free online at http://www.acog.org/~/media/Departments/Tobacco%20Alcohol%20and%20Substance%20Abuse/FASD%20Clinician%20Guide.pdf?dmc=1&ts=20120531T1400226083. Both FAS and FASDs are preventable disorders. Obstetrician–gynecologists should screen all women of reproductive age for alcohol use. Brief advice and counseling have been shown to be effective in reducing alcohol exposure during pregnancy.

American College of Obstetricians and Gynecologists. Drinking and reproductive health: a fetal alcohol spectrum disorders prevention tool kit. Washington, DC: ACOG; 2006. Available at: http://www.acog.org/~/media/Departments/Tobacco%20Alcohol%20and%20Substance%20Abuse/FASD%20Clinician%20Guide.pdf?dmc=1&ts=20120531T1400226083. Retrieved May 31, 2012.

Feldman HS, Jones KL, Lindsay S, Slymen D, Klonoff-Cohen H, Kao K, et al. Prenatal alcohol exposure patterns and alcohol-related birth defects and growth deficiencies: a prospective study. Alcohol Clin Exp Res 2012;36:670–6.

Floyd RL, O'Connor MJ, Sokol RJ, Bertrand J, Cordero JF. Recognition and prevention of fetal alcohol syndrome. Obstet Gynecol 2005;106:1059–64.

Office of Applied Studies. Alcohol use among pregnant women and recent mothers: 2002 to 2007. Rockville (MD): Substance Abuse and Mental health Services Administration; 2008. Available at: http://www.oas.samhsa.gov/2k8/pregnantAlc/pregnantAlc.pdf. Retrieved May 31, 2012.

Sokol RJ. Preventing fetal alcohol syndrome [editorial]. ACOG Clin Rev 2008;13(3):1,15–16.

94

Hepatitis C screening in pregnancy

A 30-year-old woman, gravida 2, para 1, presents for her first prenatal visit. She has a history of intravenous illicit drug use. Hepatitis C antibody is drawn with her prenatal laboratory testing. The hepatitis C antibody returns a positive test result. The patient is concerned about vertical transmission to her fetus. You inform her that the factor associated with the highest risk of vertical transmission of hepatitis C to her fetus is

(A) co-infection with hepatitis B
(B) use of fetal scalp electrode
(C) prolonged rupture of membranes
(D) elevated liver enzymes
* (E) coexistent human immunodeficiency virus (HIV) infection

Hepatitis C virus (HCV) is the most prevalent bloodborne virus in the United States and in other industrialized countries. In the general population, seropositivity for hepatitis C is approximately 2%. The highest risk group for hepatitis C is intravenous illicit drug users. In this group, the seropositivity ranges from 56% to 86%. Before 1992, the most common mode of transmission for hepatitis C was blood product transfusion. Routine screening of blood products for hepatitis C antibody has almost eliminated this transmission route to less than 1 in 1,000,000 hepatitis C infections per unit of blood. Today most people are infected through intravenous drug use.

Most acute hepatitis C infections are asymptomatic, but 70–85% of individuals will become chronically infected and 60–70% of these individuals will develop acute liver disease. Chronic hepatitis C is a very insidious virus and complications do not develop for several decades. Approximately 10–20% of individuals develop cirrhosis and 1–5% develop hepatocellular carcinoma.

Universal screening for hepatitis C in pregnancy is not recommended. The Centers for Disease Control and Prevention recommends screening of individuals at risk of bloodborne infections, ie, individuals

- with past or present history of intravenous drug abuse.
- with HIV infection.
- who received a blood transfusion or solid organ transplant before 1992.
- who received clotting factor concentrations produced before 1987.
- who have had long-term dialysis.
- who have signs or symptoms of liver disease.

The appropriate screening test is an enzyme-linked immunosorbent assay (ELISA) that detects hepatitis C antibody.

Currently, no treatment is available to reduce the risk of vertical transmission of hepatitis C to the fetus. Fortunately, the risk of congenital infections is much lower than hepatitis B and occurs in only 2–8% of neonates. Specific maternal characteristics may alter the vertical transmission rate. Detectable maternal serum HCV RNA by polymerase chain reaction test increases the risk of vertical transmission. Although a viral load of 10^6 copies is associated with a 19–22% risk of vertical transmission, a specific threshold has not been established where the risk of transmission increases. In limited studies, elevated maternal transaminases have been associated with an increased risk of vertical transmission. However, women with elevated transaminases tend to have a higher viral load. Such confounding factors have not been adequately investigated, so the effect of elevated transaminases on vertical transmission is unclear. Vertical transmission is highest (up to 30–40%) in individuals with active HCV that are co-infected with HIV. Highly active retroviral therapy likely significantly decreases the risk of vertical transmission in co-infected women. Antiviral therapy specific to hepatitis B and C is being investigated and may have potential to reduce viral transmission in the future.

Obstetric factors also may alter vertical transmission rates. Mode of delivery does not appear to alter the risk of vertical transmission. Therefore, a cesarean delivery is not recommended. In pregnant women co-infected with HIV and HCV, the HIV viral load should dictate clinical management. Prematurity and chorioamnionitis do not increase vertical transmission rate. Use of fetal scalp electrode does increase the fetal risk and should be avoided. Ruptured membranes greater than 6 hours may increase the risk of HCV infection to the fetus but the subject remains controversial. Operative vaginal delivery has not been adequately studied to recommend for or against the

procedure. In general, breastfeeding is not considered a risk factor for vertical transmission of HCV and should not be discouraged.

Airoldi J, Berghella V. Hepatitis C and pregnancy. Obstet Gynecol Surv 2006;61:666–72.

Gonik B. The role of obstetrician/gynecologists in the management of hepatitis C virus infection. Infect Dis Obstet Gynecol 2008;2008:374517.

Indolfi G, Resti M. Perinatal transmission of hepatitis C virus infection. J Med Virol 2009;81:836–43.

Lok AS, Gardiner DF, Lawitz E, Martorell C, Everson GT, Ghalib R, et al. Preliminary study of two antiviral agents for hepatitis C genotype 1. N Engl J Med 2012;366:216–24.

McIntyre PG, Tosh K, McGuire W. Caesarean section versus vaginal delivery for preventing mother to infant hepatitis C virus transmission. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD005546. DOI: 10.1002/14651858.CD005546.pub2.

Michaels AJ, Nelson DR. New therapies in the management of hepatitis C virus. Curr Opin Gastroenterol 2010;26:196–201.

Viral hepatitis in pregnancy. ACOG Practice Bulletin No. 86. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007; 110:941–56.

Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. Centers for Disease Control and Prevention [published erratum appears in MMWR Morb Mortal Wkly Rep 2011;60:18]. MMWR Recomm Rep 2010;59:1–110.

95

Disseminated intravascular coagulopathy

A healthy young woman underwent a forceps delivery of a 4,200-g infant and the repair of vaginal lacerations. She is group B *Streptococcus* positive and is currently being treated with penicillin. She is estimated to have lost 1.5 L of blood. She responds temporarily to 3 L of isotonic crystalloid and medical therapy, but a further postpartum hemorrhage necessitates exploratory laparotomy. In the operating room, a broad ligament hematoma is identified along with uterine atony, and another 3 L of blood loss is estimated. During the repair, blood pressure is maintained with another 3 L of crystalloid and 5 units of packed red blood cells. The suture line shows oozing. An intraoperative complete blood count reveals a white blood cell count of 17,000/muL, hemoglobin of 5.8 g/dL, hematocrit of 18%, and platelets of 42,000/mm^3. The most likely cause of thrombocytopenia in this patient is

(A) disseminated intravascular coagulopathy
* (B) dilutional coagulopathy
(C) hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome
(D) sepsis

Normal pregnancy physiology includes an expanded plasma volume, a decrease in systemic vascular resistance, a lower mean arterial pressure, a decrease in hematocrit, which is largely dilutional, and an increase in most coagulation factors and in platelets. The average healthy young parturient is well equipped to tolerate a degree of blood loss in the range of several hundred milliliters. However, major obstetric hemorrhage complicates approximately 0.1% of vaginal deliveries and 0.4% of cesarean deliveries. In national surveys of blood use, 6–7% of all blood products used are transfused in obstetric–gynecologic cases.

Hemorrhage represents a loss of plasma fluid, red blood cells, platelets, and clotting factors. When these losses are replaced with either isotonic crystalloid with or without packed red blood cells, volume and red cell mass do not compensate for the lost platelets and clotting factors.

Dilutional coagulopathy is defined either as a lowered platelet count or a prolonged prothrombin time. Studies of major trauma patients, which, like obstetric populations, comprise healthy young individuals who can lose considerable quantities of blood quickly, show that 34% of patients who are hemorrhaging and who receive only intravenous fluids before arrival at the hospital already have dilutional coagulopathy when they are admitted to the hospital. The probability of coagulopathy is related directly to the volume of intravenous fluids given. This has been demonstrated not only in the emergency department but also in the laboratory. Normovolemic hemodilution (in vitro) up to 60% with saline produces a coagulation factor activity level of 40% of the normal level; dilution up to 70% with saline gives a critically low factor activity of approximately 30% and a fibrinogen concentration less

than 100 mg/dL; at this point, the activated partial thromboplastin time (also known as aPTT) becomes prolonged.

Bleeding, if uncorrected, can result in levels of coagulation factors or platelets that are below the critical threshold for hemostasis. A computer simulation shows that platelets begin to drop after a loss of 25% of blood volume, and are less than 50,000 after a loss of two blood volumes; fibrinogen drops below 100 mg/dL after a loss of one blood volume; prothrombin time (PT) begins to lengthen after the loss of approximately 60% of blood volume. Microvascular bleeding begins when PT is 1.8 times the normal level or fibrinogen is less than 50 mg/dL, which is a level that is achieved with a blood loss between one and two blood volumes. Prolongation of PT is the sentinel event of dilutional coagulopathy and occurs early in hemorrhage; the key to preventing coagulopathy is plasma infusion before PT becomes inadequate for hemostasis.

Dilutional coagulopathy is, thus, the most common form of coagulopathy after hemorrhage, including obstetric hemorrhage. *Disseminated intravascular coagulation*, with which it is often confused, is defined as a situation in which pathologic clotting in the microcirculation uses up clotting factors. Disseminated intravascular coagulation may be induced by sepsis, but in obstetrics it is commonly provoked by placental complications. Thrombogenic stimuli cause uncontrolled and excessive generation of thrombin, deposition of fibrin throughout the microcirculation, platelet aggregation, and consumption of coagulation factors; plasmin is produced in excess quantities as a response to the elaboration of microthrombi, and degrades coagulation factors, fibrin, and fibrinogen. The placenta is rich in thrombin and thromboplastin, and situations that expose the placental interface cause release of these factors and predispose to disseminated intravascular coagulation. The signal condition in obstetrics is placental abruption, although release of tissue factor from damaged tissue is another stimulus.

Both types of coagulopathy are treated with replacement of clotting factors and platelets, but because disseminated intravascular coagulation is a response to an underlying condition, the underlying condition must be identified and corrected.

The appropriate response to massive hemorrhage is massive transfusion, which calls for administration of packed red blood cells, platelets, and fresh frozen plasma in a ratio approximating 1:1:1. (One unit of apheresis platelets is the equivalent of 6 units of platelets.) The administration of platelets and clotting factors early in the course of hemorrhage not only reverses clinical and subclinical coagulopathy but also is associated with improved survival. In conducting a resuscitation of this extent, it is also important to remember that hypothermia and acidosis impede coagulation dramatically, so attention to maintaining normothermia and preventing or reversing hypoperfusion improves survival. This has been most clearly demonstrated in trauma, where the combination of acidosis, hypothermia, and refractory coagulopathy after injury is called the "bloody vicious cycle." Mortality in patients in this state can be 80%.

Dilutional coagulopathy is more common than disseminated intravascular coagulation after hemorrhage. Laboratory testing to distinguish between the two conditions is difficult. A scoring system was proposed in 2001 by the Scientific and Standardization Committee on Disseminated Intravascular Coagulation of the International Society on Thrombosis and Hemostasis (Box 95-1). In the absence of a criterion standard or a single laboratory test for disseminated intravascular coagulation, this score has been demonstrated to predict mortality and to correlate highly with expert assessments.

The described patient does not have one of the classical obstetric conditions associated with disseminated intravascular coagulation, such as placental abruption or amniotic fluid embolus syndrome. Her postpartum hemorrhage appears to be surgical in nature, and disseminated

BOX 95-1

Scoring System for Overt Disseminated Intravascular Coagulopathy

1. Risk assessment: Does the patient have an underlying disorder known to be associated with overt DIC?
   - If yes, Proceed
   - If no, Do not use this algorithm
2. Order global coagulation tests (ie, platelet count, prothrombin time, fibrinogen, fibrin-related marker).
3. Score global coagulation results
   - Platelet count (greater than 100 = 0; less than 100 = 1; less than 50 = 2)
   - Elevated fibrin-related marker (eg, D-dimers, fibrin degradation products (no increase = 0; moderate increase = 2; strong increase = 3)
   - Prolonged prothrombin time (less than 3 seconds = 0; greater than 3 seconds but less than 6 seconds = 1; greater than 6 seconds = 2)
4. Calculate score
   - If 5 or greater: compatible with disseminated intravascular coagulopathy; repeat score daily
   - If less than 5: suggestive (not affirmative) of nonovert disseminated intravascular coagulopathy; repeat in the next 1–2 days

Toh CH, Hoots WK. The scoring system of the Scientific and Standardisation Committee on Disseminated Intravascular Coagulation of the International Society on Thrombosis and Haemostasis: a 5-year overview. SSC on Disseminated Intravascular Coagulation of the ISTH. J Thromb Haemost 2007;5:604–6. Copyright 2007 by Elsevier.

intravascular coagulation does not need to be invoked as the explanation for thrombocytopenia. If D-dimer testing were available intraoperatively, this might be helpful in establishing or refuting a diagnosis of disseminated intravascular coagulation, but utility of this test is hampered by the lack of consensus on what constitutes normal D-dimers in pregnancy.

Sepsis is a common underlying cause for disseminated intravascular coagulation and may be considered if thrombocytopenia occurs in a clinical context consistent with infection. The American Pregnancy Association defines *HELLP syndrome* as a series of symptoms that make up a syndrome that can affect pregnant women and, although thought to be a variant of preeclampsia, may be an entity on its own. Because the cause is still unclear, HELLP syndrome often is misdiagnosed. It is believed that HELLP syndrome affects approximately 0.2–0.6% of all pregnancies. Although HELLP syndrome requires an elevation in transaminases and lactate dehydrogenase, it may be associated with preeclampsia, disseminated intravascular coagulation, or both.

American Pregnancy Association. HELLP Syndrome [consumer information]. Irving (TX): American Pregnancy Association; 2009. Available at: http://www.americanpregnancy.org/pregnancycomplications/hellpsyndrome.html. Retrieved June 11, 2012.

Hess JR, Lawson JH. The coagulopathy of trauma versus disseminated intravascular coagulation. J Trauma 2006;60:S12–9.

Hirshberg A, Dugas M, Banez EI, Scott BG, Wall MJ Jr, Mattox KL. Minimizing dilutional coagulopathy in exsanguinating hemorrhage: a computer simulation. J Trauma 2003;54:454–63.

Ho AM, Dion PW, Cheng CA, Karmakar MK, Cheng G, Peng Z, et al. A mathematical model for fresh frozen plasma transfusion strategies during major trauma resuscitation with ongoing hemorrhage. Can J Surg 2005;48:470–8.

Maegele M, Lefering R, Yucel N, Tjardes T, Rixen D, Paffrath T, et al. Early coagulopathy in multiple injury: an analysis from the German Trauma Registry on 8724 patients. AG Polytrauma of the German Trauma Society (DGU). Injury 2007;38:298–304.

Postpartum hemorrhage. ACOG Practice Bulletin No. 76. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006;108:1039–47.

Sihler KC, Napolitano LM. Massive transfusion: new insights. Chest 2009;136:1654–67.

Thachil J, Toh CH. Disseminated intravascular coagulation in obstetric disorders and its acute haematological management. Blood Rev 2009;23:167–76.

Weiss G, Lison S, Spannagl M, Heindl B. Expressiveness of global coagulation parameters in dilutional coagulopathy. Br J Anaesth 2010;105:429–36.

96

Cervical insufficiency

A 31-year-old woman, gravida 3, comes to your office at 19 weeks of gestation with pelvic pressure. She has not experienced contractions or vaginal fluid leak. Her first pregnancy resulted in a term delivery by forceps. A large cervical defect was identified during her initial office visit at 16 weeks of gestation in her second pregnancy. She ultimately gave birth at 21 weeks of gestation secondary to painless cervical dilation. On evaluation of the current pregnancy, her uterus is soft and nontender. Speculum examination reveals a large cervical defect extending from her external os to the cervical vaginal junction. Copious white vaginal discharge with a pH less than 4.5, multiple white blood cells, and rare clue cells are seen on wet prep but yeast is absent. Her cervix is long, closed, soft, and in mid position. Transvaginal ultrasonography shows cervical funneling with a cervical length of 2.1 cm. The condition that would most likely explain these findings is

(A) bacterial vaginosis
* (B) cervical insufficiency
(C) preterm labor
(D) uterine anomaly
(E) intrauterine infection

Preterm birth, defined as delivery before 37 weeks of gestation, complicates approximately 12% of pregnancies in the United States annually. The causes of preterm birth include preterm labor (50%), preterm premature rupture of membranes (30%), and delivery for maternal or fetal indications (20%). Cervical insufficiency refers to the physical weakness of cervical tissue that is associated with painless dilation that results in preterm delivery of an otherwise healthy pregnancy, often in the second trimester. The contribution of cervical insufficiency to spontaneous preterm birth remains uncertain because an accurate diagnostic test for this condition has not been identified. Furthermore, premature cervical ripening (ie, cervical shortening) is no longer believed to be unique to cervical insufficiency because it is a common initial clinical manifestation of preterm labor.

Risk factors for true cervical insufficiency include uterine anomalies, diethylstilbestrol exposure, collagen disorders (eg, Ehlers–Danlos syndrome), dilation and curettage, cervical laceration or defect, and cervical surgery for cervical squamous cell abnormality. The described patient had a prior second-trimester delivery after painless cervical dilation accompanied by a cervical defect, and now has a short cervical length, which are findings consistent with cervical insufficiency.

Bacterial vaginosis is diagnosed when three out of four of the following findings are present: 1) 20% or more of the epithelial cells on wet mount are clue cells, 2) an abnormal gray discharge, 3) a vaginal pH greater than 4.5, and 4) a positive amine test. This patient has no evidence of bacterial vaginosis. Bacterial vaginosis is associated with an increased risk of preterm birth, however, screening for and treatment of bacterial vaginosis in women who are at risk of preterm birth remains controversial.

Preterm labor is defined as regular contractions that occur before 37 weeks of gestation and result in cervical change. This patient's history of delivery at 21 weeks of gestation after painless cervical dilation and absence of contractions in this pregnancy is most consistent with cervical insufficiency, not preterm labor.

Uterine anomalies are associated with an increased rate of preterm birth and pregnancy loss. Diagnosis usually requires direct observation at the time of cesarean delivery, laparoscopy, or an imaging study (eg, vaginal ultrasonography, hysterosalpingography, hysteroscopy, or magnetic resonance imaging). Although a uterine malformation is possible, this diagnosis cannot be assumed based on the clinical scenario described. The patient's history may warrant uterine evaluation before attempting another pregnancy. If a uterine septum is discovered, resection appears to decrease the rate of recurrent preterm delivery.

A growing body of evidence suggests that intrauterine infection leads to activation of localized inflammatory pathways, which contributes to approximately 25–40% of preterm births. An inverse relationship exists between intrauterine infection and gestational age of preterm birth based on the finding of histologic chorioamnionitis in approximately 85% of deliveries before 28 weeks of gestation compared with approximately 10% of births between 33 weeks and 36 weeks of gestation. Intrauterine colonization by vaginal and cervical microorganisms is believed to be the primary pathway that results in intrauterine infection. A leading theory that links intrauterine infection to preterm birth involves activation of the innate immune system that results in release of proinflammatory cytokines, such as interleukin-1, interleukin-6, interleukin-8, and tumor necrosis factor α. These cytokines stimulate

local release of prostaglandin and matrix metalloproteinases, which may lead to uterine contractility, cervical ripening and dilatation, and membrane rupture. The absence of uterine contractions and membrane rupture suggests that intrauterine infection is not the cause of this patient's diminished cervical length.

Antibiotic therapy for certain infections, such as asymptomatic bacteriuria, decreases the rate of premature birth. However, administration of antibiotics to women with suspected intrauterine infection, either before or during pregnancy, does not appear to be effective based on data from randomized trials. Women who receive oral azithromycin and metronidazole 4 months after preterm delivery, and every 4 months until a subsequent pregnancy, gave birth at a gestational age similar to women who received placebo. Although not statistically significant, birth at an earlier gestational age and lower birth weight was noted in women who were prescribed these antibiotics. In women who presented with preterm labor before 34 weeks of gestation, treatment with erythromycin, amoxicillin–clavulanic acid, or both had no effect on gestational age at birth compared with placebo. Therefore, administration of antibiotics to high-risk women before conception, or to women with preterm labor and intact membranes, does not appear to be justified.

Andrews WW, Goldenberg RL, Hauth JC, Cliver SP, Copper R, Conner M. Interconceptional antibiotics to prevent spontaneous preterm birth: a randomized clinical trial. Am J Obstet Gynecol 2006;194:617–23.

Bastek JA, Gomez LM, Elovitz MA. The role of inflammation and infection in preterm birth. Clin Perinatol 2011;38:385–406.

Iams JD. Cervical insufficiency. In: Creasy RK, Resnik R, Iams JD, eds. Creasy and Resnik's maternal–fetal medicine: principles and practice. 6th ed. Philadelphia (PA): Saunders Elsevier; 2009. p. 583–98.

Iams JD, Berghella V. Care for women with prior preterm birth. Am J Obstet Gynecol 2010;203:89–100.

Kenyon SL, Taylor DJ, Tarnow-Mordi W. Broad-spectrum antibiotics for spontaneous preterm labour: the ORACLE II randomised trial. ORACLE Collaborative Group. Lancet 2001;357:989–94.

Reichman DE, Laufer MR. Congenital uterine anomalies affecting reproduction. Best Pract Res Clin Obstet Gynaecol 2010;24:193–208.

97

Recurrent spontaneous abortion

A 26-year-old woman, gravida 3, para 0, visits your office for evaluation of recurrent pregnancy loss. She has had three early pregnancy losses. Her first loss was a spontaneous abortion at 9 weeks of gestation. The second loss was identified as an early demise of a normal-appearing embryo on ultrasonography at 8 weeks of gestation. Her third loss was another spontaneous abortion at 9 weeks of gestation for which karyotypic analysis was normal. Her medical history is negative for chronic illnesses or any surgery. Parental karyotypes are normal. Physical examination is unremarkable; her cervix appears normal and there are no adnexal masses palpated. In addition to testing for uterine abnormalities, her evaluation should include testing for

(A) alloimmune abnormalities
* (B) antiphospholipid syndrome
(C) diabetes mellitus
(D) inherited thrombophilia
(E) thyroid disease

Recurrent pregnancy loss, defined as three or more consecutive spontaneous abortions before 19 6/7 weeks of gestation, is a problem with a multifactorial etiology. It is a source of considerable distress for many patients due to the variety of potential causes and the limited available interventions. Approximately 1% of couples who attempt to have children will experience recurrent pregnancy loss. Most patients will experience recurrent pregnancy loss early, before 9 6/7 weeks of gestation, and many of those losses will be associated with fetal aneuploidy.

The evaluation of recurrent pregnancy loss begins with a careful history with attention to previous pregnancy outcomes, evidence of the antiphospholipid syndrome, clinical signs of diabetes mellitus or thyroid disease, and evidence of uterine anomalies. Physical examination should be directed to findings of diabetes or thyroid disease and cervical or uterine anomalies. In patients without clinical evidence of thyroid disease, diabetes, polycystic ovarian syndrome, bacterial and viral infections, and alloimmune abnormalities, routine testing for these conditions

is not recommended. In the described patient, her evaluation should include testing for antiphospholipid syndrome.

An evaluation of the uterine cavity and cervix is recommended for patients with recurrent pregnancy loss, although many of the potential anomalies identified have been found in patients with successful pregnancies. Evaluation may be performed by sonohysterography, hysterosalpingography, hysteroscopy, or magnetic resonance imaging. To date, no consensus exists on intervention for uterine anomalies. Patients for whom repair is associated with significant morbidity, such as those with a bicornuate uterus, may not benefit from intervention.

Karyotypic analysis of the parents or of a conceptus is expensive and may not be covered by insurance. If a parental karyotype abnormality is identified, treatment options are limited. If a conceptus is found to have an isolated abnormality, the subsequent pregnancy has a better prognosis, so unnecessary testing may be avoided in that case.

Testing for antiphospholipid syndrome is recommended in women with recurrent pregnancy loss. Approximately 3–15% of patients with recurrent early pregnancy loss will have antiphospholipid syndrome. The diagnosis is determined by the presence of clinical and laboratory criteria (Appendix B) and when three consecutive pregnancy losses occur before 10 weeks of gestation in patients with normal maternal and paternal chromosomes and no maternal anatomic or hormonal abnormalities. A single pregnancy loss at 10 weeks of gestation or beyond, with a fetus that is morphologically normal, is also a clinical criterion of antiphospholipid syndrome. In women with antiphospholipid syndrome and recurrent pregnancy loss, even without a history of thrombosis, treatment with heparin and low-dose aspirin may decrease the risk of subsequent pregnancy loss by 50%.

Although retrospective studies have suggested a link, there are no prospective studies that support an association between inherited thrombophilias (such as factor V Leiden and prothrombin *G20210A* gene mutation) and first-trimester pregnancy loss. Women with recurrent pregnancy losses should not be routinely tested for inherited thrombophilias. Even if an association exists between recurrent pregnancy loss and thrombophilia, insufficient evidence exists to justify preventive treatment with low molecular weight heparin or unfractionated heparin. A recent trial randomized 294 women with two previous pregnancy losses without identifiable cause to receive either intensive pregnancy surveillance alone or surveillance combined with enoxaparin and low-dose aspirin. No differences in pregnancy outcome were observed between the two groups.

When a cause for recurrent pregnancy loss cannot be identified, which is most of the time, there is a role for supportive encouragement. A large treatment trial involving women with an average of 4.2 pregnancy losses showed a 65% live birth rate in the placebo group. Although the data are limited, ultrasonographic monitoring through the first trimester with frequent visits appear to show improved outcomes.

Antiphospholipid syndrome. Practice Bulletin No. 118. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011; 117:192–9.

Branch DW, Gibson M, Silver RM. Clinical practice. Recurrent miscarriage. N Engl J Med 2010;363:1740–7.

Clark P, Walker ID, Langhorne P, Crichton L, Thomson A, Greaves M, et al. SPIN (Scottish Pregnancy Intervention) study: a multicenter, randomized controlled trial of low-molecular-weight heparin and low-dose aspirin in women with recurrent miscarriage. Blood 2010;115:4162–7.

Inherited thrombophilias in pregnancy. Practice bulletin No. 124. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:730–40.

Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295–306.

98

Vaginal birth after a cesarean delivery

A 28-year-old woman, gravida 2, para 1, at 39 weeks of gestation is undergoing a trial of labor after cesarean delivery. Her first child was a breech delivery infant weighing 3,750 g at 37 weeks of gestation, and the operative report confirms that she had a low transverse incision. This labor was spontaneous and has progressed normally. During this trial of labor, the most common sign of uterine rupture is

(A) tachysystole
(B) vaginal bleeding
* (C) worsening fetal heart rate pattern
(D) loss of fetal station
(E) new onset severe abdominal pain

Trial of labor after previous cesarean delivery (TOLAC) has had a controversial history. At one time condemned with the adage "Once a section, always a section," the 1990s saw a resurgence of the practice. As data on outcomes accumulated, cautions were raised that complications, although uncommon, were devastating. This led to a sharp decrease in the number of women who asked for TOLAC as well as the number of physicians and hospitals that offered the procedure.

Data show that a TOLAC that results in a successful vaginal birth is associated with fewer complications than a planned repeat cesarean delivery. Failed TOLAC, however, has a higher rate of serious complications than does elective repeat cesarean delivery. Successful vaginal birth after cesarean delivery can be predicted with modest accuracy based on specific maternal clinical factors (Box 98-1). A mathematical prediction model suggests that morbidity for TOLAC is at or below that of planned repeat cesarean delivery when the probability of successful vaginal birth after cesarean reaches 60–70%. Patients in this category who undergo TOLAC can be reassured that their risks are at least no greater than a repeat cesarean delivery.

Of reported TOLAC complications, the most severe is uterine rupture. Although incidence of this complication during TOLAC is quite low, it is still approximately double that of planned cesarean delivery (0.8% versus 0.4%). Because most of the studies in this area are relatively small and retrospective, the reported rates vary widely, and underreporting is likely in the case of planned cesarean deliveries. The presentation of uterine rupture may be subtle and the result can be catastrophic, thus it is generally recommended that whenever possible a team able to complete an emergency cesarean delivery be immediately available. This requirement has led many hospitals to discourage the practice of TOLAC altogether.

BOX 98-1

Selected Maternal Clinical Factors Associated With Trial of Labor After Previous Cesarean Delivery Success

Increased Probability of Success (Strong Predictors)

- Prior vaginal birth
- Spontaneous labor

Decreased Probability of Success (Other Predictors)

- Recurrent indication for initial cesarean delivery (eg, labor dystocia)
- Increased maternal age
- Non-white ethnicity
- Gestational age greater than 40 weeks
- Maternal obesity
- Preeclampsia
- Short interpregnancy interval
- Increased neonatal birth weight

Vaginal birth after previous cesarean delivery. Practice Bulletin No. 115. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:450–63.

Findings that may serve as clues to possible uterine rupture include increased frequency of contractions (tachysystole), vaginal bleeding, loss of fetal station, or new onset of intense uterine pain. The most common finding is a worsening fetal heart rate pattern, which is noted in up to 70% of cases of uterine rupture. Thus, TOLAC should not be undertaken unless continuous fetal monitoring is available. Use of other adjuncts, such as intrauterine pressure catheters, have not been shown to improve diagnostic accuracy.

Grobman WA, Lai Y, Landon MB, Spong CY, Leveno KJ, Rouse DJ, et al. Can a prediction model for vaginal birth after cesarean also predict the probability of morbidity related to a trial of labor? Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Am J Obstet Gynecol 2009;200:56.e1–6.

Grobman WA, Lai Y, Landon MB, Spong CY, Leveno KJ, Rouse DJ, et al. Development of a nomogram for prediction of vaginal birth after cesarean delivery. National Institute of Child Health and Human Development (NICHD) Maternal–Fetal Medicine Units Network (MFMU). Obstet Gynecol 2007;109:806–12.

Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW, et al. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. N Engl J Med 2004;351:2581–9.

Vaginal birth after previous cesarean delivery. Practice Bulletin No. 115. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:450–63.

99

Peripartum anticoagulation

A 27-year-old woman, gravida 3, para 2, at 34 weeks of gestation currently receives prophylactic low molecular weight heparin. She is a heterozygous carrier for the factor V Leiden mutation, with a family history of deep vein thrombosis in her mother and sister, although she has no personal history of thromboembolism. She had two prior cesarean deliveries at 38 weeks and 37 weeks of gestation and is planning to have a repeat cesarean delivery at 39 weeks of gestation. To optimize her chances for regional anesthesia in the event of an unplanned cesarean delivery, the best approach to management of her anticoagulation would be

(A) continuation of low molecular weight heparin, including on the day of surgery
(B) continuation of low molecular weight heparin and addition of protamine sulfate 2 hours before surgery
* (C) switch to prophylactic unfractionated heparin at 36 weeks of gestation
(D) discontinuation of anticoagulation at 36 weeks of gestation
(E) switch to low-dose aspirin in the week of her surgery

Because of safety, ease of dosing, and lack of fetal effects, low molecular weight heparin is the favored mode of anticoagulation for women in pregnancy. Warfarin is not recommended because of concerns of teratogenicity and fetal anticoagulation, and unfractionated heparin is less favored because of its frequent dosing and high risk of thrombocytopenia and allergic reactions.

Dosage of low molecular weight heparin is typically once daily for prophylactic purposes, whereas adjusted, weight-based dosage for therapeutic levels is typically twice daily. Adjusted-dose regimens can be managed by following anti-Xa levels, with a goal range of 0.6–1.0 units/mL, measured 4 hours after administration.

The utility of low molecular weight heparin is limited by its long half-life in comparison with unfractionated heparin. This complicates management of the pregnant patient at term. Labor and delivery present increased risks of bleeding complications. As a result, patients should be transitioned from low molecular weight heparin to unfractionated heparin at 36 weeks of gestation, or earlier if the patient is at risk of preterm delivery. The use of unfractionated heparin, with its shorter dose interval and half-life, improves the option of neuraxial analgesia and lowers the risk of hemorrhage at the time of delivery.

Protamine sulfate may be used to reverse anticoagulation due to heparin in urgent or emergent situations, although it may be less effective in the setting of low molecular weight heparin compared with unfractionated heparin. The planned use of protamine for scheduled cases is not favored. If necessary, blood products in the form of fresh frozen plasma or cryoprecipitate may be used for cases of bleeding.

With signs or symptoms of labor, a patient on anticoagulation should be instructed to withhold the next dose. In most circumstances, anticoagulation will be held through labor or at the time of cesarean delivery. Delivery that occurs 4 or more hours from the time of the most recent dose of anticoagulation is not likely to be complicated by bleeding. In most cases, neuraxial analgesia is safe 12 hours after a prophylactic dose or 24 hours after a therapeutic dose of low molecular weight heparin.

Low molecular weight heparin may be used for the entire course of pregnancy, particularly in cases where delivery is scheduled. However, because patients often

may go into labor or require delivery before 39 weeks of gestation, a switch to prophylactic unfractionated heparin at 36 weeks of gestation remains the favored approach.

Anticoagulation may be resumed 4–6 hours after vaginal delivery or 6–12 hours after cesarean delivery. Patients who are not ambulatory in the postpartum period, and who do not have a known or suspected lower extremity venous thromboembolism, should wear pneumatic compression stockings until ambulatory.

Duhl AJ, Paidas MJ, Ural SH, Branch W, Casele H, Cox-Gill J, et al. Antithrombotic therapy and pregnancy: consensus report and recommendations for prevention and treatment of venous thromboembolism and adverse pregnancy outcomes. Pregnancy and Thrombosis Working Group. Am J Obstet Gynecol 2007;197:457.e1–21.

Holst J, Lindblad B, Bergqvist D, Garre K, Nielsen H, Hedner U, et al. Protamine neutralization of intravenous and subcutaneous low-molecular-weight heparin (tinzaparin, Logiparin). An experimental investigation in healthy volunteers. Blood Coagul Fibrinolysis 1994;5:795–803.

Horlocker TT, Wedel DJ, Benzon H, Brown DL, Enneking FK, Heit JA, et al. Regional anesthesia in the anticoagulated patient: defining the risks (the second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation). Reg Anesth Pain Med 2003;28:172–97.

Inherited thrombophilias in pregnancy. Practice bulletin No. 124. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:730–40.

100

Electronic fetal heart rate monitoring management

A primiparous woman at 39 weeks of gestation has been undergoing induction for gestational hypertension. Her pregnancy was otherwise uncomplicated. Despite adequate contractions, she remained in the latent phase for 12 hours but has progressed to 4–5 cm/–1 station over the past 3 hours. Her fetal heart rate (FHR) monitor strip is shown in Fig. 100-1. A cervical re-examination shows dilation of 5 cm; her examination is otherwise unchanged. Oxytocin has been discontinued and the patient has moved to the left lateral recumbent position. Her vital signs are normal. The intervention that is most appropriate given this FHR pattern is

(A) supplemental maternal oxygen
* (B) amnioinfusion
(C) immediate cesarean delivery
(D) observation
(E) tocolytic therapy

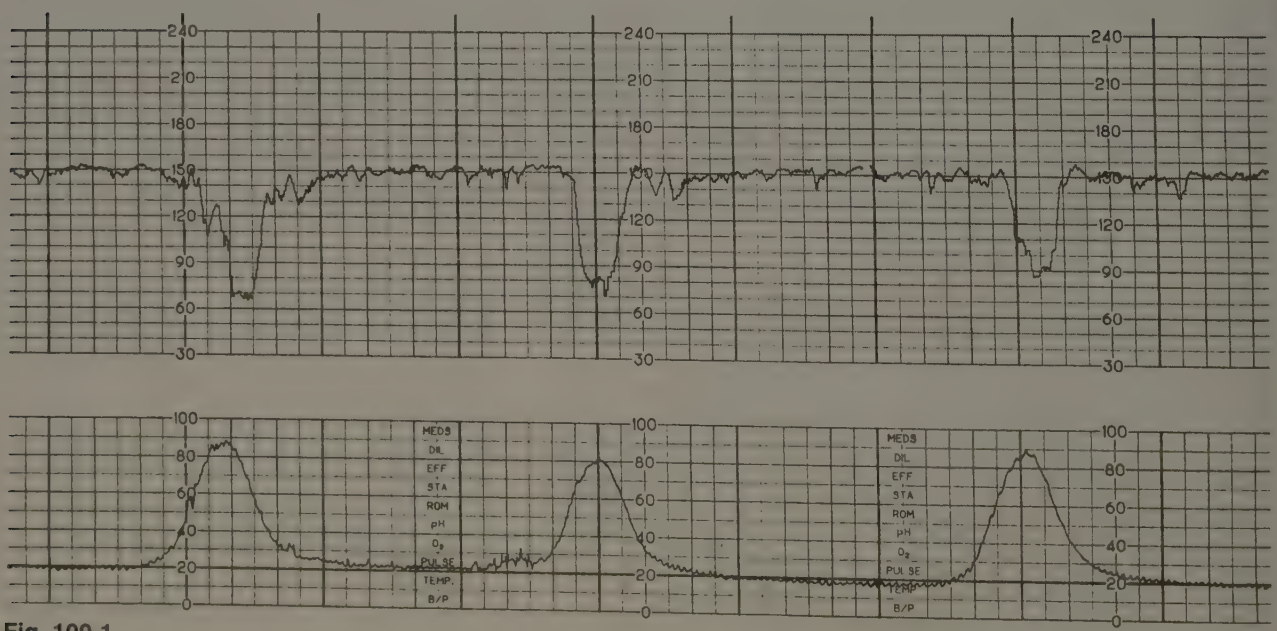


Fig. 100-1

Since the introduction of electronic fetal monitoring, there has been confusion over the proper terminology to describe FHR patterns as well as appropriate management strategies. In an effort to provide clarification, a 2008 workshop was co-sponsored by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the American College of Obstetricians and Gynecologists, and the Society for Maternal–Fetal Medicine. From this workshop, a number of publications have resulted.

The workshop led to a change in syntax regarding electronic tracings, with emphasis on physiologic significance rather than simply descriptive language. Tracings are categorized as normal (Category I), indeterminate (Category II), or abnormal (Category III), with specific guidelines for management of each category (see Appendix E-1–E-2). Despite the clarification, difficulty still remains in defining and treating the Category II tracings. These Category II tracings are defined by the 2008 workshop as not meeting criteria for either Category I or Category III, and the recommended action is "continued surveillance and reevaluation, taking into account the entire associated clinical circumstances. In some circumstances, either ancillary tests to ensure fetal well-being or intrauterine resuscitative measures may be used with Category II tracings."

Recurrent variable decelerations may represent cord compression as labor progresses and amniotic fluid diminishes. There also may be an element of vagal stimulation because of diminished fluid. Depending on the patient's progress in labor, recurrent decelerations may require no intervention. However, if they persist for a prolonged period, they may degenerate into a more ominous pattern as the fetus's compensatory capability diminishes. Although neonatal outcomes are not improved with amnioinfusion, the frequency of cesarean delivery performed for "abnormal tracings" is decreased. Therefore, amnioinfusion would be an appropriate option for managing this patient.

Although supplemental oxygen is recommended as part of the management of Category III tracings, its value is uncertain. Immediate cesarean delivery would represent a clear overreaction to this Category II strip. There is moderate variability, a stable baseline, and no tachycardia. In most cases, the presence of moderate variability or FHR accelerations ensure that the fetus is not hypoxic at that point in time. There is therefore no reason to consider this infant compromised.

Although observation alone may be elected in some instances, the presence of recurrent variable decelerations is unlikely to spontaneously revert to a Category I strip. Therefore, resuscitative measures are more commonly implemented. However, if delivery is imminent, observation may be prudent because the fetus is unlikely to become compromised over a short period. Use of tocolysis would presuppose tachysystole is responsible for the FHR tracing. The strip does not show evidence of tachysystole or evidence of recurrent variables particularly associated with tachysystole.

Chauhan SP, Klauser CK, Woodring TC, Sanderson M, Magann EF, Morrison JC. Intrapartum nonreassuring fetal heart rate tracing and prediction of adverse outcomes: interobserver variability. Am J Obstet Gynecol 2008;199:623.e1–5.

Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. ACOG Practice Bulletin No. 106. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:192–202.

Management of intrapartum fetal heart rate tracings. Practice Bulletin No. 116. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:1232–40.

Pettker CM. Standardization of intrapartum management and impact on adverse outcomes. Clin Obstet Gynecol 2011;54:8–15.

Regi A, Alexander N, Jose R, Lionel J, Varghese L, Peedicayil A. Amnioinfusion for relief of recurrent severe and moderate variable decelerations in labor. J Reprod Med 2009;54:295–302.

Westgate JA, Wibbens B, Bennet L, Wassink G, Parer JT, Gunn AJ. The intrapartum deceleration in center stage: a physiologic approach to the interpretation of fetal heart rate changes in labor. Am J Obstet Gynecol 2007;197:236.e1–11.

101

Hydramnios evaluation

A 35-year-old woman, gravida 1, comes to your office for a routine prenatal visit at 34 weeks of gestation. Her prenatal course to date has been unremarkable. Ultrasonography done at 18 weeks of gestation reported no abnormalities. She was found to be Rh negative after an initial negative antibody screen. Her 1-hour glucose challenge was 129 mg/dL. Her fundal height measures 38 cm. Ultrasonography for uterine size greater than gestational dates demonstrates an amniotic fluid index of 29 cm and isolated hydramnios. The most likely cause of this condition is

* (A) idiopathic
(B) esophageal obstruction
(C) isoimmunization
(D) gestational diabetes mellitus
(E) placental tumor

New onset hydramnios complicates 3–4% of pregnancies and often clinically presents with increased uterine size greater than expected in the third trimester. Simple ultrasonographic measures, either by four quadrant amniotic fluid index or maximum vertical pocket, can establish the presence of this problem. Although diabetes mellitus, congenital anomalies, placental tumors, and isoimmunization are all causal factors for excessive volumes of amniotic fluid, the most common cause is idiopathic, which accounts for 40–50% of cases. In regard to the described patient, two normal ultrasonographic studies with no anomalies detected make a congenital malformation or placental tumor less likely. She could have developed isoimmunization if the father of her baby is Rh positive. The diagnosis of isoimmunization is excluded given the negative maternal antibody screen. Gestational diabetes mellitus also is excluded given the normal glucose challenge test result. Idiopathic hydramnios can be associated with fetal macrosomia, and a fetal weight assessment is suggested. Hydramnios is associated with increased risk for stillbirth and antenatal testing is indicated.

Some patients with a high amniotic fluid index in the third trimester before term have such large uteri that respiratory, skeletal, and even renal consequences can result. In these patients, amnioreduction can be considered. These procedures should be done in settings where rapid delivery can be accomplished, because evacuation of volumes of amniotic fluid greater than 1,000 mL has been associated with placental abruptions. The therapeutic benefit from these procedures is short-lived and hydramnios often recurs.

Any lesion, whether mechanical or neurologic, that impairs fetal swallowing of amniotic fluid can lead to hydramnios. Obstructive lesions include esophageal atresia, tracheoesophageal fistula, and pyloric stenosis. Severe central nervous system abnormalities, such as anencephaly, hydranencephaly, or holoprosencephaly can inhibit swallowing function. All of these phenomena result in severe alterations of sonographic appearance and are seldom subtle.

Biggio JR Jr, Wenstrom KD, Dubard MB, Cliver SP. Hydramnios prediction of adverse perinatal outcome. Obstet Gynecol 1999;94:773–7.

Magann EF, Chauhan SP, Doherty DA, Lutgendorf MA, Magann MI, Morrison JC. A review of idiopathic hydramnios and pregnancy outcomes. Obstet Gynecol Surv 2007;62:795–802.

Marino T. Ultrasound abnormalities of the amniotic fluid, membranes, umbilical cord, and placenta. Obstet Gynecol Clin North Am 2004;31:177–200.

102

Seizure disorder medications

A 27-year-old woman at 7 weeks of gestation is on multiple medications to control her seizures. You counsel her that the antiepileptic drug with the highest teratogenic risk is

(A) phenytoin
* (B) valproate
(C) lamotrigine
(D) levetiracetam
(E) carbamazepine

Epilepsy is a common disorder of childbearing age. Although antiepileptic drugs are known to be associated with congenital anomalies, they should not be discontinued in patients with active epilepsy. These medications are highly effective in treating this potentially life-threatening condition. The risks of seizures to both the mother and the fetus are not inconsequential and treatment is warranted to prevent them. Trauma from seizures and status epilepticus are the leading causes of excess morbidity and mortality in women with epilepsy in pregnancy. It is common for women to stop or reduce their doses of antiepileptic drugs during pregnancy for fear of birth defects. This places the woman at increased risk of morbidity while usually not reducing the risk of teratogenesis. The greatest risk of malformations occurs during early pregnancy, before a woman may realize she is pregnant. Thus, the fetus may already have been exposed to teratogenic risk before the medication was stopped.

A number of epidemiologic studies have consistently demonstrated an increased risk of teratogenesis in women who take antiepileptic drugs. The rate in the general population is approximately 2–3% compared with 4–7% in individuals with antiepileptic drug exposure. The question of whether epilepsy itself in the absence of such drug exposure increases the risk of malformation has been raised. Recent data suggest that epilepsy without antiepileptic drug treatment is not associated with an increase in malformations.

Fetal anticonvulsive syndromes or antiepileptic drug syndromes have been associated with several of these medications, including phenytoin, valproate, carbamazepine, and phenobarbital. Characteristics of these syndromes are generally similar and include low or broad nasal bridge, epicanthal folds, hypertelorism, low hairline, and hypoplasia of distal phalanges and nails. These syndromes also may be associated with abnormal cognitive development typically when there are craniofacial anomalies. The risk of neural tube defects (NTDs) is increased with valproate exposure (1–5%) and carbamazepine (0.5–1%). Rates of malformations have been consistently shown to be increased with increasing dosages of antiepileptic drugs and with polytherapy compared with monotherapy.

Valproate appears to have the highest risk of teratogenesis, especially in dosages of more than 1,500 mg per day. Risks of malformations with exposure to phenytoin and carbamazepine are considered to be comparable with each other with the exception of the increased risk of NTDs with carbamazepine. The NTD risk with carbamazepine is lower than with valproate. A large European pregnancy and epilepsy registry study reported a lower rate of malformations with the use of lamotrigine up to one year after birth, although a dose-response effect was present (Table 102-1). A study of levetiracetam (N=117 patients) did not show an increased risk of malformations. In one study, children exposed to levetiracetam did not differ in early cognitive development compared with controls. In that study, 8% of children exposed to levetiracetam dropped below the average range of developmental quotient scores compared with 40% of children exposed to valproate.

More information is needed from ongoing registries to confirm the relative reduced risk of malformations with some of the newer antiepileptic drugs. Treatment of women with epilepsy is important for both maternal and fetal health. The use of antiepileptic drugs should be guided by the principles of monotherapy with the lowest effective dose. The use of valproate should be avoided when possible.

TABLE 102-1. Number of Offspring With Malformations for the Four Monotherapies of Different Dosages at Conception*

Medication by Dosage (mg per Day)	Sample Size	Congenital Malformation up to Birth to 2 Months Rate (95% CI)	Congenital Malformation up to 1 Year Rate (95% CI)	No. who are Seizure Free (%)
Carbamazepine				
Less than 400	148	2 (1.3%, 0.16–4.80)	5 (3.4%, 0.11–7.71)	95 (64%)
400 or more to less than 1,000	1,047	34 (3.2%, 2.26–4.51)	56 (5.3%, 4.07–6.89)	699 (67%)
1,000 or more	207	16 (7.7%, 4.48–12.25)	18 (8.7%, 5.24–13.39)	129 (62%)
Lamotrigine				
Less than 300	836	14 (1.7%, 0.92–2.79)	17 (2.0%, 1.19–3.24)	562 (67%)
300 or more	444	16 (3.6%, 2.07–5.79)	20 (4.5%, 2.77–6.87)	303 (68%)
Phenobarbital				
Less than 150	166	7 (4.2%, 1.71–8.50)	9 (5.4%, 2.51–10.04)	117 (71%)
150 or more	51	7 (13.7%, 5.70–26.26)	7 (13.7%, 5.70–26.26)	35 (69%)
Valproic acid				
Less than 700	431	18 (4.2%, 2.49–6.52)	24 (5.6%, 3.60–8.17)	306 (71%)
700 or more to less than 1,500	480	43 (9.0%, 6.56–11.88)	50 (10.4%, 7.83–13.50)	316 (66%)
1,500 or more	99	23 (23.2%, 15.33–32.79)	24 (24.2%, 16.19–33.89)	63 (63%)

* Data represent events, ie, rate, 95% CI (confidence interval), unless otherwise stated.

Reprinted from Tomson T, Battino D, Bonizzoni E, Craig J, Lindhout D, Sabers A, et al. Dose-dependent risk of malformations with antiepileptic drugs: an analysis of data from the EURAP epilepsy and pregnancy registry. EURAP study group. Lancet Neurol 2011;10:609–17.

Harden CL, Meador KJ, Pennell PB, Hauser WA, Gronseth GS, French JA, et al. Practice parameter update: management issues for women with epilepsy—focus on pregnancy (an evidence-based review): teratogenesis and perinatal outcomes: report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society. American Academy of Neurology and American Epilepsy Society. Neurology 2009;73:133–41.

Kluger BM, Meador KJ. Teratogenicity of antiepileptic medications. Semin Neurol 2008;28:328–35.

Perucca E. Birth defects after prenatal exposure to antiepileptic drugs. Lancet Neurol 2005;4:781–6.

Shallcross R, Bromley RL, Irwin B, Bonnett LJ, Morrow J, Baker GA. Child development following in utero exposure: levetiracetam vs sodium valproate. Liverpool Manchester Neurodevelopment Group; UK Epilepsy and Pregnancy Register. Neurology 2011;76:383–9.

Tomson T, Battino D, Bonizzoni E, Craig J, Lindhout D, Sabers A, et al. Dose-dependent risk of malformations with antiepileptic drugs: an analysis of data from the EURAP epilepsy and pregnancy registry. EURAP study group. Lancet Neurol 2011;10:609–17.

103

Ultrasonography to date pregnancy

A 23-year-old primigravid woman comes to your office to establish prenatal care. She has had regular menstrual cycles that she recorded in her daily calendar. Her last menstrual period dating places her at 11 3/7 weeks of gestation. She requests first-trimester aneuploidy screening. Her nuchal translucency measurement is normal, but the ultrasonographic determination of gestational age, as measured by composite biometric data, is 13 4/7 weeks. While reviewing her records, you find that she made a visit to the emergency department when she was at 7 4/7 weeks of gestation by menstrual criteria. The visit included ultrasonography that showed a singleton pregnancy with a crown–rump length consistent with 9 0/7 weeks of gestation. The parameter that will best establish gestational age for this patient is the

* (A) 9-week ultrasonography
(B) 13-week ultrasonography
(C) last menstrual period
(D) 16-week ultrasonography

The establishment of an accurate gestational age is the foundation on which rests the balance of prenatal care testing and treatment. First-trimester genetic screening requires early and accurate gestational age estimation for scheduling purposes. Maternal serum analyte screening in the second trimester and the management of pregnancies that are not delivered by 40 weeks or 41 weeks of gestation also are affected by dating assignments. In a meta-analysis of 11 randomized trials, early ultrasonography was shown to decrease labor induction for postterm pregnancy, and increase detection of multiple gestations. No reduction was observed in adverse outcomes for fetuses that had routine ultrasonography examination in early pregnancy.

A number of criteria have been evaluated in their ability to estimate gestational age. Dating is established by clinical criteria, physical examination findings, or ultrasonographic data, except in uncommon cases when in vitro fertilization dates or artificial insemination dates are available. The accuracy of clinical criteria is compounded by the variability inherent in human gestational periods and in ovulation timing. Traditionally, pregnancy is forecast to last 280 days from the first day of the last normal menstrual period, or 266 days from the date of ovulation. The implicit assumption is that all patients ovulate on day 14 of the cycle. Issues with recall bias for the date of the last menstrual period and with variability in ovulation introduce error into dating estimates based on menstruation alone. Physical examination findings have not been found to be highly accurate (plus or minus 2 weeks in the first trimester).

The American College of Obstetricians and Gynecologists recommends the following criteria to define an accurate estimate of delivery date based on ultrasonographic examination:

- Last menstrual period dating that agrees within 7 days of first-trimester crown–rump length
- Last menstrual period dating that agrees within 10 days of second-trimester composite biometry up to 20 weeks of gestation
- Mean sac diameter before 6 weeks of gestation

If last menstrual period dating does not agree with ultrasonographic findings in either of the first two cases, pregnancy dating is assigned to the ultrasonographic estimate. Caution is advised when considering reassignment of gestational age in the third trimester by ultrasonographic findings, because the error in gestational age estimation may be as high as 3 weeks or 4 weeks.

First trimester crown–rump length and maximum embryo length at 6–10 weeks of gestation are the most accurate ultrasonographic criteria for gestational age assignment. When the crown–rump length exceeds 60 mm, composite biometry should be used. Composite biometry from second-trimester ultrasonography is also highly accurate. In the third trimester, genetic variability in fetal growth limits the accuracy of ultrasonography in gestational age assignment. The third-trimester femur length is the best isolated measure of gestational age, but a 3–4-week variation in accuracy exists near term.

The 9-week crown–rump length in this case is the most accurate criterion. It cannot confirm last menstrual period dating because the difference between the two is greater than 7 days. Neither 13-week and 16-week ultrasonographic estimates nor an average of the 9-week and 13-week estimates are as accurate as a 9-week estimate.

Savitz DA, Terry JW Jr, Dole N, Thorp JM Jr, Siega-Riz AM, Herring AH. Comparison of pregnancy dating by last menstrual period, ultrasound scanning, and their combination. Am J Obstet Gynecol 2002;187:1660–6.

Whitworth M, Bricker L, Neilson JP, Dowswell T. Ultrasound for fetal assessment in early pregnancy. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: CD007058. DOI: 10.1002/14651858.CD007058.pub2.

Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;113:451–61.

104

Timing of antibiotic administration for cesarean delivery

A 21-year-old primigravid woman comes to the hospital at 38 weeks of gestation in active labor. Her genital culture for group B streptococcus is negative. Because of arrest of the active phase at 8 cm dilation, you decide to perform a cesarean delivery. Surgical antibiotic prophylaxis should be administered

* (A) before skin incision
(B) at cord clamping
(C) after peritoneal incision
(D) at skin closure

Surgical site infection prevention by preoperative antibiotic therapy has been demonstrated in nonobstetric cases. A reduction in infectious morbidity after cesarean delivery by administering prophylactic antibiotics has also been demonstrated. The timing recommendations for antibiotic prophylaxis for cesarean delivery have recently changed.

The practice of delaying antibiotic administration until cord clamping was intended to avoid concerns related to administration of antibiotics to the neonate transplacentally. These concerns were related to the presence of systemic antibiotics in neonates who might need blood cultures and other studies if sepsis were suspected. This belief has not been supported by prospective trials. Two randomized trials that examined the timing of antibiotic prophylaxis for cesarean delivery found no difference in neonatal sepsis or evaluations for sepsis between groups of infants born by cesarean delivery to women who had perioperative antibiotics administered either at skin incision or at cord clamping. Both trials also identified a decrease in endometritis in patients who received antibiotics before skin incision compared with patients who received antibiotics at cord clamping.

A first-generation cephalosporin is the most common choice for antibiotic prophylaxis for cesarean delivery. Broad-spectrum agents or multiple doses have not been shown to be more effective than single-dose cefazolin therapy. Long procedures or excessive blood loss may necessitate supplemental antibiotic doses to maintain microbicidal levels through the case. Obese patients (body mass index greater than 30) may require larger doses of antibiotic prophylaxis to achieve effective tissue concentrations. In bariatric surgery patients, a 2-g dose of cefazolin preoperatively produced the same blood and tissue concentrations of antibiotic as a 1-g dose in nonobese patients. A specific dosing algorithm for obese patients is not yet established.

In cases such as the described patient, the American College of Obstetricians and Gynecologists recommends prophylactic antibiotic administration within 60 minutes before skin incision. To delay administration until cord clamping, peritoneal incision, or closure is not as effective in preventing postpartum endometritis. With the additional time after regional anesthetic administration for preoperative skin preparation, catheter insertion, draping, and time out, the antibiotic will have time to reach target tissues. In emergency cases, the antibiotic should be administered as soon as possible.

Chauhan SP, Klauser CK, Woodring TC, Sanderson M, Magann EF, Morrison JC. Intrapartum nonreassuring fetal heart rate tracing and prediction of adverse outcomes: interobserver variability. Am J Obstet Gynecol 2008;199:623.e1–5.

Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. ACOG Practice Bulletin No. 106. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:192–202.

Management of intrapartum fetal heart rate tracings. Practice Bulletin No. 116. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:1232–40.

Pettker CM. Standardization of intrapartum management and impact on adverse outcomes. Clin Obstet Gynecol 2011;54:8–15.

105

Latent phase of labor

A 19-year-old primigravid woman presents at 37 weeks of gestation. She reports uterine contractions for the past 6 hours but appears comfortable. On external uterine monitoring, the patient is contracting irregularly every 7–15 minutes and the fetal heart rate tracing is Category I. The cervix is 1 cm dilated and 50% effaced, with a vertex presentation at –3 station. The best next step in management is

(A) oxytocin administration
(B) prostaglandin administration
(C) artificial rupture of membranes
* (D) observation

Clinically, the beginning of labor is very difficult to define. By strict definition, labor starts when uterine contractions cause effacement and dilation of the cervix. In reality, patients often experience contractions that may or may not cause cervical change. Contractions associated with false labor tend to have different characteristics than those associated with true labor, as shown in Table 105-1. However, the distinction between true and false labor often requires time and serial cervical examinations. If the cervix remains unchanged over time, the most likely diagnosis is false labor. However, if cervical change is documented, the probable diagnosis is labor.

If the described patient is in labor, she would be in the latent phase of stage 1. The latent phase is defined as the time from the onset of regular uterine contractions until approximately 4–6 cm cervical dilation. The course and duration of labor in nulliparous women is slower than in multiparous women. The duration of the latent phase of labor in nulliparous patients usually is less than 20 hours, and in multiparous patients it is usually less than 14 hours. These cutoffs describe the fifth percentile for labor progression, meaning that 95% of parturients will progress more quickly than described in the Friedman curve. A patient is diagnosed with a prolonged latent phase if she exceeds this timeline.

The best choice for the care of this patient is observation to await more active labor. If the patient is extremely uncomfortable, administration of a narcotic or sleeping medication may be useful (ie, the so-called "therapeutic rest"). Labor induction with oxytocin, prostaglandin, or artificial rupture of membranes is not indicated in the management of a normal latent phase of labor because it may increase the risk of cesarean delivery.

Dystocia and augmentation of labor. ACOG Practice Bulletin No. 49. American College of Obstetricians and Gynecologists. Obstet Gynecol 2003;102:1445–54.

Induction of labor. ACOG Practice Bulletin No. 107. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:386–97.

Zhang J, Troendle J, Mikolajczyk R, Sundaram R, Beaver J, Fraser W. The natural history of the normal first stage of labor [published erratum appears in Obstet Gynecol 2010;116:196]. Obstet Gynecol 2010;115:705–10.

Zhang J, Troendle JF, Yancey MK. Reassessing the labor curve in nulliparous women. Am J Obstet Gynecol 2002;187:824–8.

TABLE 105-1. Characteristics of Contractions in False Labor and True Labor

Contraction Characteristic	False Labor	True Labor
Contraction timing	Contractions are irregular and do not become more frequent	Contractions come at regular intervals and increase in frequency
Positional changes	Contractions may stop with walking, resting, or change in position	Contractions continue despite movement
Strength	Contractions are usually mild and do not increase in strength	Contractions increase steadily in strength
Pain	Pain usually is felt only in the front	Pain usually starts in the back and moves to the front

106

Placenta previa at 20 weeks of gestation

A 32-year-old woman, gravida 4, para 3, comes to see you for a routine anatomical survey at 21 weeks of gestation. Her pregnancy has been uncomplicated thus far. She is healthy and has had three prior vaginal deliveries at term. The anatomical survey is normal and the fetus shows normal growth. An anterior placenta previa is suspected transabdominally. The next most appropriate management step would be to perform

(A) color flow Doppler ultrasonography
(B) magnetic resonance imaging (MRI)
(C) repeat transabdominal ultrasonography in 2 weeks
* (D) transvaginal ultrasonography
(E) three-dimensional ultrasonography

Placenta previa refers to a placenta that overlies or abuts the internal os of the cervix. Most cases of placenta previa are suspected during routine transabdominal ultrasonography in the second trimester. The incidence of previa during the second trimester on transabdominal ultrasonography is reported to be in the range of 5–20% whereas the incidence at term is less than 0.5% of pregnancies. The false-positive rates and false-negative rates range from 2% to 25% for diagnosis of a placenta previa by transabdominal ultrasonography. To see important landmarks, such as the cervical os, on transabdominal ultrasonography, the bladder must be distended. Bladder distention results in approximation of the anterior and posterior walls of the lower uterine segment. Thus, a normally situated placenta may be distorted and appear to cover the internal os.

The preferred approach to diagnose placenta previa in the second trimester is transvaginal ultrasonography. Neither three-dimensional ultrasonography nor MRI has such a role in the diagnosis of placenta previa. Color flow Doppler ultrasonography is helpful to identify a vasa previa but not a placenta previa. Transvaginal ultrasonography improves the diagnostic accuracy because the bladder is empty, fetal parts do not obscure views of the placental edge, and resolution is much higher in the visualization of the cervix and placental edge. With transvaginal ultrasonography, the incidence of placenta previa during the second trimester is greatly reduced to approximately 1–4% of pregnancies. This imaging technique does not increase the risk of bleeding.

A placenta previa diagnosed in the second trimester at an anatomical scan should be followed up at 28–32 weeks of gestation with ultrasonography. The later in pregnancy that ultrasonography confirms placenta previa, the more unlikely the placenta previa is to resolve. Risk factors for persistent placenta previa are a prior cesarean delivery, advanced gestation at diagnosis, and the amount of the placenta that overlaps the cervix. If the previa persists, a cesarean delivery is the recommended mode of delivery.

A patient who has a placenta previa detected during the second trimester should be informed that she is at risk of vaginal bleeding. A cervical length at or after 24 weeks of gestation in a woman with a placenta previa is useful in predicting patients at highest risk for adverse outcomes and may be considered. A transvaginal cervical length of 30 mm or less in a woman with placenta previa is associated with an increased risk of hemorrhage, uterine activity, and preterm birth. The patient should seek immediate medical attention if vaginal bleeding occurs. After bleeding occurs, the physician may recommend that the patient avoid exercise and intercourse; however, the benefit of these recommendations has not been substantiated by research.

Placenta previa is the primary risk factor for a placenta accreta. The risk of an accreta with a placenta previa and no prior cesarean delivery is approximately 3%. The incidence of accreta is increased by a prior cesarean delivery and an anterior previa. As the number of cesarean deliveries increases, so does the risk of an accreta.

Diagnosis of placenta accreta is often, but not always, made by prenatal ultrasonography. Specific ultrasonographic markers are a loss of the hypoechoic myometrial–placental interface, multiple hypoechoic spaces within the placenta, and color flow Doppler ultrasonography demonstrating vascular flow adjacent to the bladder. Small areas of abnormal placental invasion may be particularly difficult to see. Obesity and other technical factors may compromise ultrasonographic visualization. In the absence of a standard criterion (other than posthysterectomy pathology), it is difficult to ascertain test performance, but sensitivity of ultrasonography for diagnosis of placenta accreta has been reported to be 77–97%.

Magnetic resonance imaging has been suggested as an ancillary test when placenta accreta is suspected; MRI appears to have a higher positive predictive value and a lower negative predictive value than ultrasonography. At this time, the routine use of MRI is not recommended, although it may be helpful if ultrasonography is inconclusive.

Bhide A, Thilaganathan B. Recent advances in the management of placenta previa. Curr Opin Obstet Gynecol 2004;16:447–51.

Cho JY, Lee YH, Moon MH, Lee JH. Difference in migration of placenta according to the location and type of placenta previa. J Clin Ultrasound 2008;36:79–84.

Ghi T, Contro E, Martina T, Piva M, Morandi R, Orsini LF, et al. Cervical length and risk of antepartum bleeding in women with complete placenta previa. Ultrasound Obstet Gynecol 2009;33:209–12.

Stafford IA, Dashe JS, Shivvers SA, Alexander JM, McIntire DD, Leveno KJ. Ultrasonographic cervical length and risk of hemorrhage in pregnancies with placenta previa. Obstet Gynecol 2010;116:595–600.

Vergani P, Ornaghi S, Pozzi I, Beretta P, Russo FM, Follesa I, et al. Placenta previa: distance to internal os and mode of delivery. Am J Obstet Gynecol 2009;201:266.e1–5.

107

Fish intake in pregnancy

A 25-year-old woman, gravida 2, visits your office at 14 weeks of gestation for advice about nutrition during her pregnancy. You advise her that the U.S. Food and Drug Administration (FDA) has studied mercury levels in king mackerel, salmon, swordfish, tilefish, and tuna. You tell her that the FDA found that the fish likely to have the lowest mercury level is

(A) king mackerel
* (B) salmon
(C) swordfish
(D) tilefish
(E) tuna

Mercury, accumulated in a biologically available form called methylmercury, is associated with childhood learning and memory deficits as well as delays in cognitive performance. The principal route of mercury exposure is through fish consumption. Exposure to mercury in prenatal patients also may be associated with hydrocephaly, cleft palate, heart defects, and preterm birth. The safety threshold for blood levels of mercury according to the Environmental Protection Agency is 5.8 micrograms/L. Some studies suggest that mercury concentrations in cord blood are higher than in maternal blood, which has led experts to propose a lower maximum threshold of 3.5 micrograms/L. The general consensus appears to be that there is no actual safe level of mercury exposure for the fetus.

Fish consumption also carries benefits. Fish are a chief source of omega-3 fatty acids, which are important in neonatal brain and eye development. Many of the studies that examine neurodevelopmental traits in children born to women with high levels of fish consumption are confounded by the simultaneous risk of mercury exposure and benefit of increased levels of omega-3 fatty acids.

Mercury accumulates in predatory fish that live for longer periods of time than the species they consume. Pelagic fish, such as sharks, swordfish, and tuna, are especially prone to concentrate mercury in their tissues. Methylmercury concentrations in humans will decrease slowly and may take 1 year or more to return to baseline levels after fish consumption is modulated. For this reason, during preconception counseling, patients should be advised about recommendations for fish consumption.

The FDA has determined that average total mercury levels in salmon range from 0.014 ppm to undetectable (less than 0.01 ppm). Therefore, salmon is the fish with the lowest mercury level that you should advise this patient to consider above other options. King mackerel (0.730 ppm), swordfish (0.976 ppm), tilefish from the Gulf of Mexico (1.450 ppm), and shark (0.988 ppm) have unacceptably high levels of mercury for regular consumption during pregnancy. Tuna mercury levels are more variable. Canned light tuna contains 0.118 ppm of mercury. Canned albacore tuna contains 0.353 ppm, and fresh tuna, whether species-specific or unknown, ranges from 0.205 ppm to 0.639 ppm in mercury content.

Freshwater fish may have high mercury levels as well, so patients should be advised to check with regional health departments regarding fish caught locally.

Fish intake in pregnancy should be restricted because of the potential effect of methylmercury toxicity. A total of 340 g (12 oz) per week, or approximately two servings, of fish and shellfish low in mercury is recommended. The recommended intake of albacore or other non-light tuna species is 170 g (6 oz) per week, or approximately one serving.

Food and Drug Administration. Mercury levels in commercial fish and shellfish (1990–2010). Washington, DC: FDA; 2011. Available at:http://www.fda.gov/food/foodsafety/product-specificinformation/seafood/foodbornepathogenscontaminants/methylmercury/ucm115644.htm. Retrieved June 11, 2012.

Miranda ML, Edwards S, Maxson PJ. Mercury levels in an urban pregnant population in Durham County, North Carolina. Int J Environ Res Public Health 2011;8:698–712.

Mulligan ML, Harris WS. Should pregnant women eat fish? J Reprod Med 2009;54:263–6.

Oken E, Radesky JS, Wright RO, Bellinger DC, Amarasiriwardena CJ, Kleinman KP, et al. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort. Am J Epidemiol 2008;167:1171–81.

Ramon R, Ballester F, Aguinagalde X, Amurrio A, Vioque J, Lacasana M, et al. Fish consumption during pregnancy, prenatal mercury exposure, and anthropometric measures at birth in a prospective mother–infant cohort study in Spain. Am J Clin Nutr 2009;90:1047–55.

108

Nausea and vomiting in pregnancy

A 30-year-old woman, gravida 2, para 1, comes to see you for a prenatal visit and tells you that she has persistent nausea and vomiting, particularly early in the day. She is at 8 weeks of gestation and has a normal intrauterine pregnancy on ultrasonography. She has been taking vitamin B_6 for 2 weeks since finding out she was pregnant, and has not had any weight changes. Urine dipstick test result is negative for ketones, her pulse is normal, and orthostatic measurements are normal. The most appropriate next step for treatment is

(A) intravenous fluids
(B) parenteral nutrition
* (C) doxylamine succinate
(D) methylprednisolone
(E) ondansetron hydrochloride

Nausea and vomiting of pregnancy affects most pregnant women in the first trimester, with 70–80% experiencing nausea and 50% experiencing episodes of vomiting. Symptoms can progress and become more difficult to treat if they are not treated early. *Hyperemesis gravidarum*, which occurs in fewer than 2% of pregnancies, is commonly defined as persistent vomiting in the setting of dehydration, electrolyte changes (eg, hypokalemia), ketosis, and weight loss of greater than 5%. Severe nausea and vomiting of pregnancy constitutes the third most common reason for hospitalization in pregnancy. Any time moderate to severe nausea and vomiting occurs during pregnancy, other systemic conditions should be considered and ruled out.

Mild nausea and vomiting in the first trimester is often self-limited and can be controlled with behavior modification. Many pregnant women are sensitive to particular stimuli that may provoke nausea and vomiting and avoidance of these stimuli is often the first step to improvement. In particular, avoidance of spicy foods and iron supplements is suggested. Some physicians recommend changing to frequent and small meals, focusing on a bland, dry diet that is rich in protein. Drinking clear and cold liquids between meals can also be helpful.

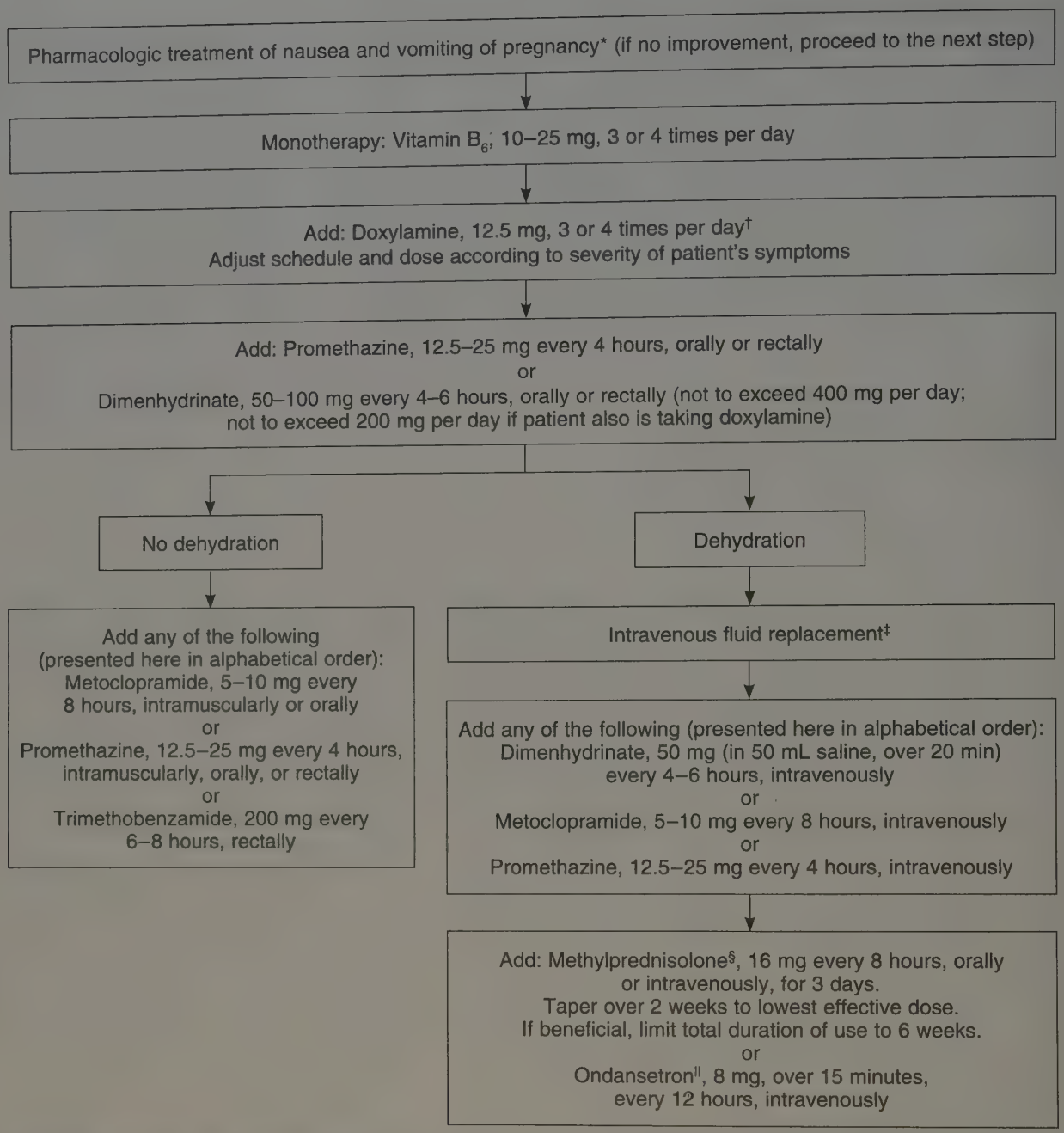
Early and aggressive treatment helps prevent worsening of nausea and vomiting. Nonpharmacologic therapies often are suggested early in pregnancy. A multivitamin may prove a useful preventive measure if administered before symptomatology in the periconceptional period. Several trials support the use of ginger for treatment of nausea and vomiting in pregnancy. There is mixed evidence for use of devices that give pressure or stimulation to the P6 acupressure point on the wrist, but this simple and easily remembered tool may be helpful for some patients.

Use of pharmacologic therapies is guided by a balance between effectiveness and safety. A useful algorithm based on this principle is shown in Figure 108-1. Vitamin B_6 is considered a first-line treatment for nausea and vomiting in pregnancy because of proven effectiveness in two separate trials, as well as its safety and low risk of adverse effects. Doxylamine succinate is an antihistamine (H1 receptor blocker) that is often added to a regimen of vitamin B_6. Available as an over-the-counter sleep medication in the United States, one half of a 25-mg tablet taken 3–4 times daily is associated with a 70% reduction in nausea and vomiting in randomized trials and patients can be reassured that studies have demonstrated no evidence of adverse fetal effects.

Dimenhydrinate (another antihistamine), promethazine hydrochloride (a phenothiazine), metoclopramide hydrochloride or trimethobenzamide hydrochloride (both dopamine agonists) may be tried in succession in patients who fail to respond to the combination of vitamin B_6 and doxylamine. Ondansetron hydrochloride, a 5-t-3 (5-hydroxytryptamine) receptor antagonist, has shown great effectiveness in nausea and vomiting related to chemotherapy and is being used more frequently for pregnancy. One trial has shown equal effectiveness to promethazine, but with less sedating effects (see Fig. 108-1).

Limited data are available on the effectiveness of corticosteroids (eg methylprednisolone) in reducing nausea and vomiting. However, multiple studies have demonstrated a dose-related twofold to threefold increased risk of facial clefting if used before 10 weeks of gestation. As a result, use of glucocorticoids should be reserved for refractory cases.

This patient does not show signs of dehydration or hyperemesis requiring hydration or supplemental nutrition. Intravenous fluids (with supplemental multivitamins


Pharmacologic treatment of nausea and vomiting of pregnancy* (if no improvement, proceed to the next step)
Monotherapy: Vitamin B6, 10–25 mg, 3 or 4 times per day
Add: Doxylamine, 12.5 mg, 3 or 4 times per day†
Adjust schedule and dose according to severity of patient's symptoms
Add: Promethazine, 12.5–25 mg every 4 hours, orally or rectally
or
Dimenhydrinate, 50–100 mg every 4–6 hours, orally or rectally (not to exceed 400 mg per day; not to exceed 200 mg per day if patient also is taking doxylamine)
No dehydration
Dehydration
Add any of the following (presented here in alphabetical order):
Metoclopramide, 5–10 mg every 8 hours, intramuscularly or orally
or
Promethazine, 12.5–25 mg every 4 hours, intramuscularly, orally, or rectally
or
Trimethobenzamide, 200 mg every 6–8 hours, rectally
Intravenous fluid replacement‡
Add any of the following (presented here in alphabetical order):
Dimenhydrinate, 50 mg (in 50 mL saline, over 20 min) every 4–6 hours, intravenously
or
Metoclopramide, 5–10 mg every 8 hours, intravenously
or
Promethazine, 12.5–25 mg every 4 hours, intravenously
Add: Methylprednisolone§, 16 mg every 8 hours, orally or intravenously, for 3 days.
Taper over 2 weeks to lowest effective dose.
If beneficial, limit total duration of use to 6 weeks.
or
Ondansetron‖, 8 mg, over 15 minutes, every 12 hours, intravenously

*This algorithm assumes other causes of nausea and vomiting have been ruled out. At any step, consider parenteral nutrition if dehydration or persistent weight loss is noted. Alternative therapies may be added at any time during the sequence depending on patient acceptance and clinician familiarity; consider P6 acupressure with wrist bands or acustimulation or ginger capsules, 250 mg four times daily.

†In the United States, doxylamine is available as the active ingredient in some over-the-counter sleep aids; one half of a scored 25-mg tablet can be used to provide a 12.5-mg dose of doxylamine.

‡Thiamine, intravenously, 100 mg daily for 2–3 days (followed by intravenous multivitamins), is recommended for every woman who requires intravenous hydration and has vomited for more than 3 weeks. No study has compared different fluid replacements for nausea and vomiting of pregnancy.

§Corticosteroids appear to increase risk for oral clefts in the first 10 weeks of gestation.

‖Safety, particularly in the first trimester of pregnancy, has not yet been determined; less effect on nausea.

FIG. 108-1. Pharmacologic treatment of nausea and vomiting of pregnancy. (Nausea and vomiting of pregnancy. ACOG Practice Bulletin No. 52. American College of Obstetricians and Gynecologists. Obstet Gynecol 2004;103: 803–14.)

and thiamine) are typically reserved for patients who cannot tolerate any oral intake for a prolonged period or when dehydration is apparent. Enteral or parenteral feeding should be reserved for the most intractable cases given their difficulty and risk. Total parenteral nutrition, for instance, has a 25% risk of line sepsis and can contribute to significant hepatic disease.

Matthews A, Dowswell T, Haas David M, Doyle M, O'Mathúna DP. Interventions for nausea and vomiting in early pregnancy. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD007575. DOI: 10.1002/14651858.CD007575.pub2; 10.1002/14651858.CD007575.pub2.

Nausea and vomiting of pregnancy. ACOG Practice Bulletin No. 52. American College of Obstetricians and Gynecologists. Obstet Gynecol 2004;103:803–14.

Niebyl JR. Clinical practice. Nausea and vomiting in pregnancy [published erratum appears in N Engl J Med 2010;363:2078]. N Engl J Med 2010;363:1544–50.

109

Amniotic fluid embolus

A 26-year-old primigravid woman is undergoing induction of labor for severe preeclampsia at 39 weeks of gestation. She has an epidural catheter in place and is on a continuous infusion of a local anesthetic. She is receiving magnesium sulfate for seizure prophylaxis at 2 g/hour. She has sudden cardiac collapse and the anesthesiologist believes that she has had an amniotic fluid embolus. The most common presenting symptom of amniotic fluid embolus is

(A) ventricular arrhythmia
(B) coagulopathy
(C) sinusoidal fetal heart rate pattern
(D) hematuria
* (E) maternal hypoxemia

Profound changes in maternal oxygenation represent a consistent presenting symptom in patients with amniotic fluid embolus, also known as anaphylactoid syndrome of pregnancy. Although amniotic fluid embolus is rare, it has catastrophic consequences for the mother and child. Mortality rates range from 50% to 80%. Acute pulmonary hypertension is thought to be due to spasm and subsequent hypertension of the pulmonary artery. Changes in the maternal heart rhythm or sinusoidal fetal heart rate patterns are later manifestations that are a function of the original hypoxemic insult, and are nonspecific for amniotic fluid embolus. Coagulopathy is a delayed finding and only present in women who survive the initial presentation of low oxygen levels. Changes in coagulation appear hours after the initial insult. Hematuria is not sensitive or specific for amniotic fluid embolus.

Given that maternal hypoxemia is the first manifestation of amniotic fluid embolus, first steps in management should include intubation and positive pressure ventilation with 100% oxygen. Anesthesia personnel should intubate and oxygenate, obstetricians should effect delivery when safe to do so, and consultants in critical care, blood banking, and hematology should be consulted. Given the low prevalence of amniotic fluid embolus (1–10 per 100,000 deliveries), most clinicians have never seen a patient with this condition.

Other causes for respiratory arrest in a healthy parturient include magnesium toxicity, total spinal anesthesia, and cerebrovascular accident. Magnesium sulfate toxicity is associated with hyporeflexia and a slow decrease in respiratory rate. Total spinal anesthesia leads to loss of consciousness and paralysis of all extremities. Cerebrovascular accidents often have localizing neurologic deficits. None of these other conditions have as part of their presentation the severe coagulopathy that amniotic fluid embolus often exhibits.

Magnesium sulfate toxicity is the condition that causes respiratory arrest in laboring women that is the easiest to reverse. Parenteral infusions of calcium gluconate or carbonate quickly and predictably restore breathing. This antidote to excessive magnesium sulfate infusion or impaired maternal clearance should be readily available in all clinical settings where magnesium sulfate is infused.

Conde-Agudelo A, Romero R. Amniotic fluid embolism: an evidence-based review. Am J Obstet Gynecol 2009;201:445.e1–13.

Gist RS, Stafford IP, Leibowitz AB, Beilin Y. Amniotic fluid embolism. Anesth Analg 2009;108:1599–602.

Kretzschmar M, Zahm DM, Remmler K, Pfeiffer L, Victor L, Schirmeister W. Pathophysiological and therapeutic aspects of amniotic fluid embolism (anaphylactoid syndrome of pregnancy): case report with lethal outcome and overview. Anaesthesist 2003;52:419–26.

McDonnell NJ, Muchatuta NA, Paech MJ. Acute magnesium toxicity in an obstetric patient undergoing general anaesthesia for caesarean delivery. Int J Obstet Anesth 2010;19:226–31.

Montagnana M, Franchi M, Danese E, Gotsch F, Guidi GC. Disseminated intravascular coagulation in obstetric and gynecologic disorders. Semin Thromb Hemost 2010;36:404–18.

110

Cervical length

A 22-year-old primigravid woman at 20 weeks of gestation was found to have a cervical length of 26 mm with funneling noted at her routinely scheduled anatomic survey. A repeat ultrasonographic scan 2 weeks later revealed a cervical length of 15 mm. She has experienced no contractions, vaginal bleeding, or leakage of vaginal fluid. Speculum examination was negative for membrane rupture or prolapsed membranes. Her cervix is soft and closed on pelvic examination. The best next step in management is

(A) bed rest
(B) cerclage placement
(C) intramuscular progesterone
(D) repeat cervical length in 1 week
* (E) vaginal progesterone

Preterm delivery is the major cause of perinatal and infant morbidity and mortality in nonanomalous births. A cervical length of 2.5 cm or less is associated with an increased risk of preterm delivery, even in women without a prior preterm birth. Furthermore, the risk of preterm delivery becomes greater as the cervical length decreases.

In a randomized trial, administration of micronized vaginal progesterone, 200 mg nightly from 24 weeks to 34 weeks of gestation was associated with a 45% reduction in the rate of delivery before 34 weeks of gestation in asymptomatic women with a cervical length of 15 mm or less. Similar findings were noted in another randomized trial with the use of vaginal progesterone gel in asymptomatic women with a cervical length of 10–20 mm at 19.0/7–23 6/7 weeks of gestation. Both of these studies revealed benefit in women without a prior preterm birth. Therefore, vaginal progesterone is the best choice for the described patient.

The use of intramuscular 17-α-hydroxyprogesterone caproate in women with a prior preterm birth and cervical length less than 25 mm reduced the rate of previable delivery and perinatal mortality but not the rate of preterm birth in women at less than 35 weeks of gestation. Currently, there are no data to support the use of 17-α-hydroxyprogesterone caproate in asymptomatic nulliparous women with a short cervix.

Bed rest is not recommended because data are lacking to support its efficacy. Furthermore, bed rest may cause harm by decreasing maternal muscle mass and increasing the risk of thromboembolism. Repeating cervical length assessment in 1 week is not the best next step because the described patient already meets the criteria for vaginal progesterone therapy. Cerclage does not appear to decrease the rate of preterm delivery in asymptomatic women who have a short cervix but who have not had a prior preterm birth. A recent randomized trial demonstrated that use of a pessary in a woman with a short cervix is useful but further studies may be necessary.

Berghella V, Figueroa D, Szychowski JM, Owen J, Hankins GD, Iams JD, et al. 17-Alpha-Hydroxyprogesterone Caproate for the Prevention of Preterm Birth in Women with Prior Preterm Birth and a Short Cervical Length. Vaginal Ultrasound Trial Consortium. Am J Obstet Gynecol 2010;202:351.e1–6.

Fonseca EB, Celik E, Parra M, Singh M, Nicolaides KH. Progesterone and the risk of preterm birth among women with a short cervix. Fetal Medicine Foundation Second Trimester Screening Group. N Engl J Med 2007;357:462–9.

Goya M, Pratcorona L, Merced C, Rodó C, Valle L, Romero A, et al. Cervical pessary in pregnant women with a short cervix (PECEP): an

open-label randomised controlled trial. Pesario Cervical para Evitar Prematuridad (PECEP) Trial Group. Lancet 2012;379:1800–6.

Hassan SS, Romero R, Vidyadhari D, Fusey S, Baxter JK, Khandelwal M, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. PREGNANT Trial. Ultrasound Obstet Gynecol 2011;38:18–31.

Iams JD, Berghella V. Care for women with prior preterm birth. Am J Obstet Gynecol 2010;203:89–100.

Sosa C, Althabe F, Belizán JM, Bergel E. Bed rest in singleton pregnancies for preventing preterm birth. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.: CD003581. DOI: 10.1002/14651858.CD003581.pub2.

111

Maternal complications of sickle cell anemia

A 24-year-old African American woman, gravida 2, para 1, at 18 weeks of gestation with known sickle cell anemia comes to the hospital with a 1-day history of cough and fever. On physical examination, her respiratory rate is 20 breaths per minute and her temperature is 38.8°C (101.8°F). Her oxygen saturation by pulse oximetry is 94% on room air. Her pulmonary examination is normal. Her chest X-ray reveals an infiltrate in the left lower lobe. Fetal heart tones are 180 beats per minute. Her examination is otherwise normal. Her blood pressure, heart rate, and urine output are normal. The most likely diagnosis is

(A) sepsis
(B) pulmonary embolism
* (C) acute chest syndrome
(D) pulmonary hypertension

Sickle cell disease is an autosomal recessive disease involving hemoglobin S. The defect in the hemoglobin results in repetitive episodes of hemolysis and vasoocclusion. Hemolysis occurs as the result of repeated episodes of polymerization–depolymerization as red blood cells pick up and release oxygen into the circulation. The red blood cell membrane is also more fragile, so the life expectancy of the red blood cell is decreased. Both issues lead to anemia. Intermittent vascular occlusion causes acute and chronic organ dysfunction from inflammation and ischemia-reperfusion injuries. Complications from end organ damage occur. These complications decrease life expectancy in individuals with sickle cell disease. The only known disease-modifying drug is hydroxyurea. Hydroxyurea is contraindicated during pregnancy because it may increase the risk of congenital malformations and stillbirth. Most treatment for sickle cell disease is supportive. Supportive treatment includes oxygen therapy, intravenous hydration, pain control, and blood transfusion when indicated.

Pain constitutes the most common cause for individuals to seek medical attention. Painful crisis can occur with or without precipitating factors. Any precipitating factors should be treated and the pain managed aggressively. Nonsteroidal antiinflammatory drugs cannot be used in pregnancy for prolonged pain management and should be used cautiously in patients with renal disease. The mainstay of pain management during pregnancy is acetaminophen and narcotics. Caution should be used not to exceed the maximum daily dose of acetaminophen. In a patient with liver dysfunction, acetaminophen should be used sparingly, if at all. All narcotics can cause mild to severe central nervous system depression in the fetus. Prolonged use of meperidine should be avoided in pregnancy because normeperidine, an active metabolite with a long half-life of 63 hours, can accumulate in the fetus. Long-term narcotic use in pregnancy may lead to neonatal abstinence syndrome. The benefit to the maternal health and well-being must be weighed against the fetal risk.

Pulmonary complications of sickle cell disease are common and acute chest syndrome is the second most common reason for patients with sickle cell disease to seek medical care. Acute chest syndrome is diagnosed by new pulmonary infiltrate with chest pain, temperature greater than 38.5°C (101.3°F), and tachypnea, wheezing, or cough. The causes of acute chest syndrome are infection, pulmonary infarction, and fat embolism. Acute chest syndrome should be recognized early and treated aggressively because it is a major cause of mortality in adults with sickle cell disease. Management of acute chest syndrome includes standard blood transfusion for mild hypoxemia and exchange transfusion for moder-

ate to severe hypoxemia. Aggressive pulmonary toilet should be implemented with either incentive spirometry or bronchodilators in patients who are wheezing. Mechanical ventilation may be required for supportive care. Broad spectrum antibiotics that include coverage for atypical organisms should be administrated because approximately one half of patients will have an underlying infection. The most common respiratory pathogens in patients with acute chest syndrome include *Chlamydia pneumonia*, *Mycoplasma pneumonia*, and respiratory syncytial virus. Acute chest syndrome can be associated with pulmonary hypertension. The degree of pulmonary hypertension is an independent risk factor for mortality.

Patients with sickle cell disease can develop pulmonary hypertension. The mechanism is not fully understood but chronic oxygen desaturation, repeated episodes of acute chest syndrome, recurrent thromboembolism, and high pulmonary blood flow due to anemia may be factors. Clinical symptoms of pulmonary hypertension include fatigue, dizziness, dyspnea on exertion, chest pain, and syncope. On physical examination, the second heart sound may be increased in intensity. Right ventricular enlargement also can be seen on chest X-ray. The mean survival after the diagnosis is approximately 24 months. Patients with pulmonary hypertension and sickle cell disease are treated the same as patients with primary pulmonary hypertension.

Sepsis should always be considered in sickle cell patients with a fever. Signs and symptoms include fever, shaking chills, lethargy, malaise, and hypotension. This patient is unlikely to be septic because her blood pressure, heart rate, and urine output remain clinically stable. Patients with sickle cell disease are functionally asplenic and are susceptible to overwhelming infections and sepsis with encapsulated organisms, such as *Pneumococcus* and *Haemophilus*. For this reason, a pneumococcal vaccination is recommended for all patients with sickle cell disease.

Pregnancy increases the risk of thromboembolic disease in any woman but particularly in women with sickle cell disease. The patient can experience chest pain, shortness of breath, cough, tachypnea, and tachycardia. The diagnosis and treatment of a pulmonary embolism is the same in patients with and without sickle cell disease. In this patient with fever and normal pulse oximetry, the diagnosis of pulmonary embolism is less likely.

Alhashimi D, Fedorowicz Z, Alhashimi F, Dastgiri S. Blood transfusions for treating acute chest syndrome in people with sickle cell disease. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD007843. DOI: 10.1002/14651858.CD007843.pub2.

Dauphin-McKenzie N, Gilles JM, Jacques E, Harrington T. Sickle cell anemia in the female patient. Obstet Gynecol Surv 2006;61:343–52.

Laurie GA. Acute chest syndrome in sickle cell disease. Intern Med J 2010;40:372–6.

Neville KA, Panepinto JA. Pharmacotherapy of sickle cell disease. 18th Expert Committee on the Selection and Use of Essential Medicines, March 21–25, 2011. Geneva: World Health Organization; 2011. Available at: http://www.who.int/selection_medicines/committees/expert/18/applications/Sicklecell.pdf. Retrieved June 10, 2012.

Rogers DT, Molokie R. Sickle cell disease in pregnancy. Obstet Gynecol Clin North Am 2010;37:223–37.

Stuart MJ, Setty BN. Acute chest syndrome of sickle cell disease: new light on an old problem. Curr Opin Hematol 2001;8:111–22.

112

Patient in labor with human immunodeficiency virus

A 37-year-old woman, gravida 5, para 4, at 39 weeks of gestation comes to the labor and delivery department in early labor. Her examination is consistent with a 3.2-kg estimated fetal weight. She received no prenatal care and has had no medical care since the delivery of her last child 6 years ago. She gave birth to all of her children vaginally and reports no pregnancy complications. With respect to screening for maternal human immunodeficiency virus (HIV) infection, the best management option is to offer

(A) maternal testing after delivery
* (B) rapid enzyme-linked immunosorbent assay (ELISA) HIV testing in labor
(C) rapid immediate ELISA testing of the neonate
(D) immediate maternal Western blot testing

The Centers for Disease Control and Prevention (CDC) estimates that 20% of HIV-positive individuals in the United States do not know that they are HIV infected. Current CDC recommendations are for all individuals aged 13–64 years to be screened in a health care setting and for high-risk individuals to be screened annually. The rationale for HIV testing and engaging infected individuals in care is to initiate therapy before immune function is compromised. After the individual becomes symptomatic, medical intervention is less effective. Additionally, identification allows the individual with HIV the opportunity to protect their sexual partners from infection.

For the pregnant woman, identification of HIV infection allows intervention to avoid transmission of HIV infection to her child through use of medications, appropriate use of cesarean delivery, and avoidance of breastfeeding.

Optimal antiretroviral treatment for the prevention of mother-to-child HIV transmission includes oral combination antiretroviral therapy antepartum to suppress viral replication in the maternal bloodstream, intrapartum intravenous zidovudine infusion, and zidovudine syrup to be given to the neonate for the first 6 weeks of life. For women with a detectable HIV viral load (greater than 1,000 copies/mL) near term, a cesarean delivery before labor and ruptured membranes can be used to aid in preventing transmission. Risk of mother-to-child HIV transmission can be reduced from 30% to less than 2% with optimal therapy. Any component of the outlined interventions decreases the risk of HIV transmission for the neonate.

Although HIV testing laws vary from state to state, the CDC recommends that HIV testing be included in routine prenatal laboratory panels with an option for the woman to opt out. Repeat testing in the third trimester is recommended in areas with high incidence of HIV infection (17 cases or more per 100,000 person-years or 1 in 1,000 hospital discharges) or in those who engage in behaviors with increased risk (ie, injection drug use, history of multiple sexually transmitted diseases, or sex with HIV-positive partners). For a pregnant woman who has not been tested earlier in pregnancy, rapid testing in labor and delivery should be performed unless she chooses not to undergo testing. The rapid screen is an ELISA test, which can be done in a laboratory or as a point of care test. The CDC suggests that all hospitals offering maternity care be capable of providing rapid testing for HIV. The results can be used for intrapartum treatment until diagnostic ELISA and Western blot tests can be done. Antenatal testing is preferable, however, if this is not performed, rapid ELISA testing can be performed immediately postpartum on the mother or on the neonate. The Western blot test is not a screening test but a confirmatory test.

The U.S. Public Health Service recommends that the parturient first diagnosed with HIV in labor receive intravenous zidovudine as soon as available. Other more readily available antiretroviral medications that cross the placenta and have been shown to decrease neonatal infection rates include oral zidovudine in combination with lamivudine and nevirapine. After the mother receives intrapartum therapy, the neonate should receive zidovudine syrup, preferably administered in the first 12 hours of life. Further research is needed on whether additional drugs benefit the neonate born to a sub-optimally treated mother.

For women with a positive rapid test result for HIV in labor or after rupture of membranes, it is unclear if cesarean delivery conveys protective benefit for the prevention of transmission to the neonate and decisions must be tailored to the clinical situation. Avoidance of artificial rupture of membranes, scalp electrodes, or other interventions that might increase fetal contact with maternal secretions or blood, or break the fetal skin may decrease infection risk. In the United States, breastfeeding is discouraged

because it contributes to an increased risk of infection. Postpartum, additional testing should confirm maternal HIV infection status and the woman should receive infectious disease care as well as support and counseling.

Branson BM, Handsfield HH, Lampe MA, Janssen RS, Taylor AW, Lyss SB, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. Centers for Disease Control and Prevention. MMWR Recomm Rep 2006;55:1,17; quiz CE1–4.

Jamieson DJ, Cohen MH, Maupin R, Nesheim S, Danner SP, Lampe MA, et al. Rapid human immunodeficiency virus-1 testing on labor and delivery in 17 US hospitals: the MIRIAD experience. Am J Obstet Gynecol 2007;197:S72–82.

Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1_infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. Washington, DC: United States Department of Health and Human Services; 2011. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Retrieved June 10, 2012.

Prenatal and perinatal human immunodeficiency virus testing: expanded recommendations. ACOG Committee Opinion No. 418. American College of Obstetricians and Gynecologists. Obstet Gynecol 2008;112:739–42.

113

Inherited thrombophilia

A 25-year-old white woman, gravida 1, comes to your office for a new obstetrics visit. Review of her medical record reveals a history of a spontaneous deep venous thrombosis (DVT) this past year after an ankle fracture and immobilization. She received 6 months of anticoagulation but no further evaluation. The inherited thrombophilia that is most frequently identified in patients with DVT is

(A) protein C deficiency
* (B) factor V Leiden mutation
(C) prothrombin *G20210A* gene mutation
(D) protein S deficiency
(E) antithrombin III deficiency

Inherited thrombophilias are associated with thromboembolic events both inside and outside of pregnancy. More than 20% of nonpregnant patients with DVT and no obvious precipitating factors will be diagnosed with an inherited thrombophilia after screening. Inherited thrombophilias (most commonly factor V Leiden mutation, prothrombin *G20210A* gene mutation, and protein S, protein C, and antithrombin III deficiencies) are found at varying rates in the general population. A carrier with no prior or family history of clot has a moderately increased risk of thromboembolism in pregnancy, whereas a prior history confers a much greater risk.

Factor V Leiden mutation is the most commonly identified inherited thrombophilia. It occurs in 1–15% of the general population with higher rates in individuals with European ancestry. The mutation confers resistance to proteolysis by activated protein C and can be carried in heterozygous or homozygous states. For women with factor V Leiden heterozygosity and a personal or family history of clot, the risk of thrombosis is approximately 10% in pregnancy. For women with factor V Leiden homozygosity and a personal or family history of clot, the risk of thrombosis is approximately 17% in pregnancy (Table 113-1).

Prothrombin gene mutation increases circulating prothrombin levels. This mutation is the second most common inherited thrombophilia. Outside of pregnancy, prothrombin *G20210A* gene mutation increases the risk of venous thromboembolism twofold to fourfold. Similar to factor V Leiden mutation, a prior history of venous thromboembolism in the presence of prothrombin gene mutation greatly increases the risk of venous thromboembolism. Factor V Leiden–prothrombin *G20210A* gene double heterozygosity increases the risk to more than 20% in the case of prior thromboembolism (Table 113-1).

Methylene tetrahydrofolate reductase mutation can be associated with elevated homocysteine levels, which are a risk factor for the formation of venous clots. Alone, methylene tetrahydrofolate reductase mutation does not significantly predispose to venous thromboembolism. This mutation is common in the general population and does not provide additional useful information in the care of people with thromboembolism.

Antithrombin III deficiency is an uncommon inherited thrombophilia but it carries a more substantial risk of venous thromboembolism than the others listed. Although this is among the most dangerous inherited thrombophilias, it is uncommon.

TABLE 113-1. Risk of Venous Thromboembolism With Different Thrombophilias

	Prevalence in General Population (%)	VTE Per Pregnancy (No History) (%)	VTE Per Pregnancy (Previous VTE) (%)	Out of All VTE (%)
Factor V Leiden heterozygote	1–15	Less than 0.3	10	40
Factor V Leiden homozygote	Less than 1	1.5	17	2
Prothrombin gene heterozygote	2–5	Less than 0.5	Greater than 10	17
Prothrombin gene homozygote	Less than 1	2.8	Greater than 17	0.5
Factor V Leiden–prothrombin gene double heterozygote	0.01	4.7	Greater than 20	1–3
Antithrombin III activity (less than 60%)	0.02	3–7	40	1
Protein C (less than 50%)	0.2–0.4	0.1–0.8	4–17	14
Protein S free antigen (less than 55%)	0.03–0.13	0.1	0–22	3

Adapted from Inherited thrombophilias in pregnancy. Practice bulletin No. 124. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:730–40.

Inherited thrombophilia screening can be considered in women with a personal history of thromboembolism. Some health care providers use these results to determine intensity and length of anticoagulation in pregnancy. Screening for an inherited thrombophilia as an etiology of pregnancy complications is controversial.

Inherited thrombophilias in pregnancy. Practice bulletin No. 124. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:730–40.

James AH, Jamison MG, Brancazio LR, Myers ER. Venous thromboembolism during pregnancy and the postpartum period: incidence, risk factors, and mortality. Am J Obstet Gynecol 2006;194:1311–5.

Recommendations from the EGAPP Working Group: routine testing for Factor V Leiden (R506Q) and prothrombin (20210G>A) mutations in adults with a history of idiopathic venous thromboembolism and their adult family members. Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Genet Med 2011;13:67–76.

Scifres CM, Macones GA. The utility of thrombophilia testing in pregnant women with thrombosis: fact or fiction? Am J Obstet Gynecol 2008;199:344.e1–7.

114

Contraindication to trial of labor after cesarean delivery

A patient at 39 weeks of gestation comes to the hospital with mild preeclampsia for possible labor induction. She has had two prior low transverse cesarean deliveries although the last one required a T-shaped incision. Ultrasonography 1 week ago showed the fetal weight to be 4,300 g. Her Bishop score is 5. The major contraindication to trial of labor after cesarean delivery (TOLAC) for this patient is

(A) labor induction
* (B) prior T-shaped incision cesarean delivery
(C) suspected macrosomia
(D) two prior low transverse cesarean deliveries

The rate of vaginal birth after cesarean delivery (VBAC) decreased from a high of 28.3% in the mid-1990s to 8.5% in 2006. Many hospitals in the United States, out of fear of litigation or from lack of resources, have stopped offering TOLAC altogether. In the same time interval (from the 1990s to 2006), the cesarean delivery rate rose from 20% to 31.1%, prompting the National Institutes of Health to recommend that organizations facilitate access to TOLAC for eligible patients. The benefits of VBAC in avoiding major abdominal surgery, with corresponding decreases in hemorrhage and infection, are clear. In addition, VBAC avoids cumulative effects of repeat cesarean deliveries, including increasing risk of visceral injury and abnormal placentation in future pregnancies.

Patients should be counseled about TOLAC during prenatal care with ample opportunity for questions and discussion. In addition, health care providers should be familiar with resources in their health care system that affect their ability to offer TOLAC safely.

The latest guidelines for TOLAC include all of the aforementioned options except for patients with a prior T-shaped uterine incision. The major morbidity associated with TOLAC is uterine rupture. In patients with major uterine scarring related to transfundal surgery, previous uterine rupture, classical cesarean delivery, or T-shaped uterine incision, TOLAC is generally not recommended.

Patients with an indication for labor induction may pursue TOLAC. Spontaneous labor is associated with the lowest rupture rate, but the increase in rupture from labor induction is small and may be worth the potential benefit. Labor induction with misoprostol should be avoided except in the case of second-trimester pregnancy termination or second-trimester induction for an intrauterine fetal demise. In the case of such second-trimester deliveries, the outcomes are comparable to those of patients with an unscarred uterus and reported rupture rates are less than 1%. Oxytocin and mechanical methods, such as transcervical Foley catheter insertion have some supporting data as induction agents and can be considered. A clear recommendation for or against prostaglandin E_2 for labor induction is difficult to make because of limited data.

Although macrosomia is associated with a higher rate of cesarean delivery, it should not be considered a contraindication to TOLAC, especially given the difficulty in establishing a diagnosis of macrosomia before birth. Women with macrosomic fetuses have lower success rates with TOLAC than women with normal-weight fetuses.

Patients with twin gestations and one previous cesarean delivery are candidates for TOLAC. The success rate appears to be similar to that for singleton pregnancies without any increase in uterine rupture, maternal, or neonatal morbidity.

In patients with two previous cesarean deliveries, the success rate of TOLAC is similar to the success rate after one previous cesarean delivery. Studies show a small increase in morbidity for women with more than one previous scar, but data on rupture rates are mixed. Careful consideration should be given to the reasons why the first two procedures were done in patients who are now seeking TOLAC after two previous cesarean deliveries.

Counseling should also include an examination of those factors, which increase the likelihood of successful TOLAC. Prior vaginal birth suggests a higher success rate and lower rate of maternal morbidity. Ultrasonographic examination of the lower uterine segment may eventually prove useful in identifying candidates with low risk of uterine rupture.

Landon MB. Predicting uterine rupture in women undergoing trial of labor after prior cesarean delivery. Semin Perinatol 2010;34:267–71.

Scifres CM, Rohn A, Odibo A, Stamilio D, Macones GA. Predicting significant maternal morbidity in women attempting vaginal birth after cesarean section. Am J Perinatol 2011;28:181–6.

Vaginal birth after previous cesarean delivery. Practice Bulletin No. 115. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:450–63.

115

Intimate partner violence

A 38-year-old college professor has a 6-week-twin gestation after embryo transfer. Her medical history includes asthma and depression. On routine prenatal screening, she discloses ongoing physical abuse by her husband. The factor most strongly associated with intimate partner violence is the woman's

(A) asthma
(B) infertility
* (C) depression
(D) socioeconomic status

Intimate partner violence is a common, serious, and potentially preventable health problem. It can occur between heterosexual and same-sex, married, and unmarried couples and former partners. In addition to physical harm, intimate partner violence also includes sexual and psychological harm. The Centers for Disease Control and Prevention has defined intimate partner violence as physical, sexual, and psychological abuse according to the following parameters:

- Physical violence is the intentional use of physical force with the potential to cause disability, injury, harm, or death.
- Sexual violence is in three categories: 1) use of force to compel an individual to engage in a sexual act against his or her will; 2) attempted or completed sex act involving an individual who is unable to understand the nature and condition of the act; and 3) abusive sexual conduct.
- Psychological and emotional violence and abuse involves trauma caused by threats or coercive tactics. It also includes humiliating, controlling, isolating, and denying the victim access to money or other resources.

The incidence of intimate partner violence is difficult to determine because of a bias against disclosure. Anonymous surveys are thought to give the best estimate. In a comprehensive national telephone survey of adults in the United States, 1 in 4 women and 1 in 7 men reported a lifetime prevalence of physical or sexual violence. When psychological violence was included, the estimates were much higher. Crime victim surveys grossly underestimate intimate partner violence because only a fraction of these incidents are reported to law enforcement agencies. Based upon data from the National Violent Death Reporting System, the Centers for Disease Control and Prevention estimates that there were 1,200 intimate partner violence homicides in 2005, a rate of 1.5 per 100,000 individuals; most victims were women.

The incidence of intimate partner violence in pregnancy has been reported to range from 1% to 20% and to occur across all socioeconomic strata. Violence may begin early in pregnancy and may escalate throughout the pregnancy. The postpartum period is a particularly vulnerable time for increasing intimate partner violence. Homicide related to intimate partner violence is a leading cause of maternal mortality, accounting for 13–24% of all deaths in pregnancy. Intimate partner violence also is associated with other adverse outcomes in pregnancy. Risks of spontaneous abortion, preterm labor, hypertensive disorders of pregnancy, vaginal bleeding, placental abruption, severe nausea and vomiting, dehydration, and premature rupture of membranes have all been reported to be increased in women who are victims of intimate partner violence in pregnancy.

The American College of Obstetricians and Gynecologists recommends screening all women for intimate partner violence at the first prenatal visit, in each trimester, and in the postpartum period. Several screening tools exist with no single tool being ideal. Nonetheless, the use of a simple screening tool, such as the four-question "HITS questionnaire," may be useful to the clinician (Table 115-1). The HITS questionnaire asks respondents how often their partner physically **H**urt them, **I**nsulted them, **T**hreatened them with harm, and **S**creamed at them.

Certain red flags should raise the clinician's suspicion for intimate partner violence, eg, late or no prenatal care, missed appointments, and cancelled appointments on short notice. Individual risk factors include young age, prior history of intimate partner violence, sexual assault, childhood abuse, heavy alcohol or drug use, depression, unemployment, short interpregnancy interval, and unplanned pregnancy. African American and Native American women are at increased risk of intimate partner violence. Although victims of intimate partner violence experience significant effects on their general physical and mental health, asthma and infertility have not been

TABLE 115-1. "HITS"—A Domestic Violence Tool for Use in the Community

HITS tool for intimate partner violence screening. Please read each of the following activities and fill in the circle that best indicates the frequency with which your partner acts in the way depicted.

How often does your partner?	Never	Rarely	Sometimes	Fairly often	Frequently
Physically hurt you	O	O	O	O	O
Insult or talk down to you	O	O	O	O	O
Threaten you with harm	O	O	O	O	O
Scream or curse at you	O	O	O	O	O
	1	2	3	4	5

The HITS questionnaire asks respondents how often their partner physically **H**urt them, **I**nsulted them, **T**hreatened them with harm, and **S**creamed at them. Each item is scored from 1 to 5. Thus, scores for this inventory ranged from 4 to 20. A score of greater than 10 is considered positive.

Sherin KM, Sinacore JM, Li, XQ, Zitter RE, Shakil A. HITS: a short domestic violence screening tool for use in a family practice setting. Fam Med 1998;30:508–12. The HITS screening tool is copyright 2003 by Kevin M. Sherin, MD, MPH. For permission to use HITS, e-mail kevin_sherin@doh.state.fl.us. HITS is used globally in multiple languages.

reported as specific risk factors. By contrast, depression has been identified as a risk factor of intimate partner violence.

Kiely M, El-Mohandes AA, El-Khorazaty MN, Blake SM, Gantz MG. An integrated intervention to reduce intimate partner violence in pregnancy: a randomized controlled trial [published erratum appears in Obstet Gynecol 2011;117:1232]. Obstet Gynecol 2010;115:273–83.

Sherin KM, Sinacore JM, Li XQ, Zitter RE, Shakil A. HITS: a short domestic violence screening tool for use in a family practice setting. Fam Med 1998;30:508–12.

Yost NP, Bloom SL, McIntire DD, Leveno KJ. A prospective observational study of domestic violence during pregnancy. Obstet Gynecol 2005;106:61–5.

Zolotor AJ, Denham AC, Weil A. Intimate partner violence. Obstet Gynecol Clin North Am 2009;36:847–60, xi.

116

Maternal hypothyroidism

A 24-year-old woman, gravida 1, para 0, comes to your office for her first prenatal visit. In your review of her past and current medical histories, the condition that would lead you to screen her for hypothyroidism is

(A) obesity
(B) hypertension
* (C) type 1 diabetes mellitus
(D) systemic lupus erythematosus

At this time, routine thyroid testing during pregnancy is not recommended, and only patients at risk of hypothyroidism should be screened. In pregnancy, patients should be screened with thyroid-stimulating hormone (TSH) and free thyroxine (free T_4) or free thyroxine index if the TSH is abnormal. Indications for screening include symptoms of hypothyroidism, autoimmune disorders, such as type 1 diabetes mellitus, and a personal history of thyroid disease. The initial and often indolent signs and symptoms of hypothyroidism are constipation, fatigue, hair loss, dry skin, cold intolerance, muscle cramps, prolonged relaxation phase of the deep tendon reflexes, and carpal tunnel syndrome. As hypothyroidism becomes more severe, the individual may experience weight gain, intellectual slowness, voice changes, and insomnia. If hypothyroidism is left untreated, myxedema and a myxedema coma may occur.

Hashimoto disease is one of the most common causes of hypothyroidism. Patients with Hashimoto disease produce thyroid antimicrosomal and antithyroglobulin antibodies. If a patient has one autoimmune disorder of the endocrine system, such as type 1 diabetes mellitus, her risk of having another autoimmune disorder is increased. Therefore, patients with autoimmune disorders of the endocrine system should be routinely screened. Although systemic lupus erythematosus is an autoimmune disorder, it does not affect the endocrine system.

Both the thyroid gland itself and thyroid function test results change during pregnancy. The thyroid gland can increase in size. If the thyroid gland increases in size, the change is diffuse and is not in discrete areas. Although the thyroid function is not altered, the thyroid function test results are different in euthyroid pregnant patients compared with euthyroid nonpregnant patients. Thyroid-binding globulin increases during pregnancy, so that the overall total amounts of T_4 and triiodothyronine increase while free T_4 and free triiodothyronine remain the same. Thyroid-stimulating hormone may transiently be lower in the first trimester relative to elevated human chorionic gonadotrophin levels but remains unchanged in the second trimester and third trimester.

Patients with hypothyroidism fail to produce adequate thyroid hormone. Although other thyroid preparations are available, the treatment of choice for hypothyroidism is oral replacement with levothyroxine. Patients with overt hypothyroidism are replaced with sufficient quantity of levothyroxine to normalize the TSH levels; these levels will respond approximately 4 weeks after a dose adjustment.

Thyroid replacement requirements increase during pregnancy because of the increase in thyroxine-binding globulin. On average, the amount of oral replacement increases by 40–50% during pregnancy. The greatest change in thyroxine-binding globulin occurs before 20 weeks of gestation, so the largest increases in oral replacement occur during this time. To determine if a patient with hypothyroidism is adequately replaced, she should be monitored with TSH and free T_4 or a free thyroxine index. The goal of therapy is to normalize TSH and to maintain normal free T_4 levels. In the postpartum period, thyroxine-binding globulin decreases to nonpregnant levels, so the amount of thyroid replacement requirements may need to be decreased.

Iodine deficiency can be the underlying etiology for hypothyroidism because iodine is essential to produce thyroid hormone. During pregnancy women are at increased risk of iodine deficiency. Renal clearance of iodine increases because of the increased glomerular filtration rate, the demand for iodine by the thyroid gland increases, and the fetus requires iodine from maternal stores. In industrialized countries where table salt is iodized, iodine deficiency is usually not problematic, but as women decrease their daily salt intake, iodine deficiency may become more common. Supplementation during pregnancy with a multivitamin containing 220–250 micrograms of iodine is recommended.

Routine screening of overweight individuals for hypothyroidism is not recommended during pregnancy. Hypertension has not been associated with hypothyroidism.

Burman KD. Controversies surrounding pregnancy, maternal thyroid status, and fetal outcome. Thyroid 2009;19:323–6.

Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol 2005;105:239–45.

Cleary-Goldman J, Malone FD, Lambert-Messerlian G, Sullivan L, Canick J, Porter TF, et al. Maternal thyroid hypofunction and pregnancy outcome. Obstet Gynecol 2008;112:85–92.

de Escobar GM, Obregón MJ, del Rey FE. Iodine deficiency and brain development in the first half of pregnancy. Public Health Nutr 2007;10:1554–70.

de Escobar GM, Obregón MJ, del Rey FE. Maternal thyroid hormones early in pregnancy and fetal brain development. Best Pract Res Clin Endocrinol Metab 2004;18:225–48.

Subclinical hypothyroidism in pregnancy. ACOG Committee Opinion No. 381. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;110:959–60.

Thyroid disease in pregnancy. ACOG Practice Bulletin No. 37. American College of Obstetricians and Gynecologists. Obstet Gynecol 2002;100:387–96.

117

Cervical length

A nulliparous patient at 22 weeks of gestation undergoes transabdominal ultrasonography that indicates a cervical length of 2.0 cm. No dynamic changes are observed and the fetal size is consistent with dates. The best next step in management is

(A) fetal fibronectin
(B) uterine tocodynamometry
(C) digital cervical examination
(D) review of preterm labor symptoms
* (E) transvaginal ultrasonography

The relationship between short cervical length and risk of preterm birth has been studied with the use of transvaginal ultrasonography. Introduction of the vaginal transducer allows better imaging of the cervix and lower uterine segment than does transabdominal ultrasonography. Moreover, bladder filling for transvaginal ultrasonography better enables cervical length assessment compared with transabdominal ultrasonography.

If an abnormality in cervical length is suspected transabdominally, it is reasonable to perform transvaginal ultrasonography to confirm or reject that suspicion and precisely assess the cervix. Growing evidence indicates that progestogen therapy may play a role in reducing the risk of spontaneous preterm birth in women with a shortened cervix, but trials to date have demonstrated effectiveness only when the shortening was detected by transvaginal ultrasonography.

It appears that vaginal progesterone is more effective at reducing risk of preterm birth in women who have a short cervix. Intramuscular progesterone may offer a similar advantage when the risk factor is prior preterm birth. The biology that underlies these differences and the mechanisms by which progestogen reduces some subtypes of preterm birth risk are yet to be elucidated.

Fetal fibronectin is often present in cervicovaginal secretions before 22 weeks of gestation and, thus, is of little use at this stage of pregnancy. Digital cervical examinations often miss the dilation and effacing of the cervix that occurs from internal os to the external cervical os. Neither self-report of uterine activity nor tocodynamometric assessment improves the prediction of early delivery. Nor does such knowledge afford effective prevention.

Although a woman with a shortened cervix and prior spontaneous preterm birth may well benefit from cerclage placement, it appears that progesterone therapy alone has benefit in a nulliparous woman with a short cervix. Therefore, progesterone would be the first line treatment in this patient. The role of cerclage remains to be elucidated in nulliparous women.

Dodd JM, Crowther CA. The role of progesterone in prevention of preterm birth. Int J Womens Health 2010;1:73–84.

Hassan SS, Romero R, Vidyadhari D, Fusey S, Baxter JK, Khandelwal M, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. PREGNANT Trial. Ultrasound Obstet Gynecol 2011;38:18–31.

Meijer-Hoogeveen M, Stoutenbeek P, Visser GH. Methods of sonographic cervical length measurement in pregnancy: a review of the literature. J Matern Fetal Neonatal Med 2006;19:755–62.

Norman JE, Mackenzie F, Owen P, Mactier H, Hanretty K, Cooper S, et al. Progesterone for the prevention of preterm birth in twin pregnancy (STOPPIT): a randomised, double-blind, placebo-controlled study and meta-analysis. Lancet 2009;373:2034–40.

Saul LL, Kurtzman JT, Hagemann C, Ghamsary M, Wing DA. Is transabdominal sonography of the cervix after voiding a reliable method of cervical length assessment? J Ultrasound Med 2008;27:1305–11.

118

Induction of labor

A 30-year-old woman, gravida 3, para 2, comes to your office for a routine prenatal visit at 37 weeks of gestation. Gestational dating was determined by 10-week ultrasonography. She has had an uncomplicated pregnancy, but is concerned about the timing of her delivery. She would like to discuss the option of induction of labor. Her last child was born at term within 1 hour of her feeling contractions. She lives more than 60 km (37 mi) away from the hospital. Today, she has no contractions and reports normal fetal movements. On examination, her cervix is 2 cm dilated, 60% effaced, midposition, and of soft consistency, with the fetal station being –2. The most appropriate approach to management of this pregnancy would be

(A) induction of labor today
* (B) induction of labor at 39 weeks of gestation
(C) amniocentesis for fetal lung maturity
(D) membrane stripping

More than 20% of pregnancies in the United States involve induction of labor, a rate that has more than doubled in the past 20 years. Although some of the increase is because of medically indicated inductions, nonmedically indicated cases account for a larger relative proportion of the increase.

Logistic reasons (eg, living some distance from the hospital, a history of rapid labor, or other social reasons) are acceptable indications for induction, as long as particular gestational age criteria are met (Box 118-1). Other factors that should be taken into account when counseling a patient about induction are parity and the state of cervical ripening. For instance, a nulliparous patient with an unfavorable cervix may have a relatively unacceptable risk of cesarean delivery for this particular indication.

BOX 118-1

Confirmation of Term Gestation

- Ultrasonographic measurement at less than 20 weeks of gestation supports gestational age of 39 weeks or greater.
- Fetal heart tones have been documented as present for 30 weeks by Doppler ultrasonography.
- It has been 36 weeks since a positive serum or urine human chorionic gonadotropin pregnancy test result.

Induction of labor. ACOG Practice Bulletin No. 107. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:386–97.

Recent evidence has demonstrated that nonmedically indicated delivery before 39 weeks of gestation is associated with increased morbidity—including respiratory complications, hypoglycemia, hyperbilirubinemia, sepsis, prolonged hospitalization, and admission to a newborn special care unit—even in the presence of documented biochemical fetal lung maturity by amniocentesis (Table 118-1). Documentation of fetal lung maturity by amniocentesis does not eliminate all risk. The indication for delivery must be carefully considered when counseling a patient. In the described patient, where timing of delivery is requested but is not necessarily indicated, induction of labor at 37 weeks of gestation adds risk of early term delivery, even in the setting of documented fetal lung maturity by amniocentesis.

Induction of labor or provoking labor through the common practice of membrane stripping in this patient, particularly in the absence of meeting appropriate maturity or dating criteria, would not be indicated. This patient should be reassured, prepared for the signs and symptoms of labor, and a timed delivery at or after 39 weeks of gestation can be considered.

TABLE 118-1. Neonatal Outcomes After Demonstrated Fetal Lung Maturity Before 39 Weeks of Gestation Versus Outcomes in Neonates Born at 39–40 Weeks of Gestation

	36–38 Weeks of Gestation With Documented Lung Maturity	39–40 Weeks of Gestation	Adjusted Odds Ratio (95% Confidence Interval)
Composite adverse outcome	6.1%	2.5%	1.7 (1.1–2.6)
Respiratory distress syndrome	1.5%	0.04%	7.6 (2.2–26.6)
Respiratory support	3.3%	1.1%	2.0 (1.1–3.6)
Surfactant use	0.4%	0.05%	6.4 (1.04–41)
Sepsis	5.9%	2.3%	1.7 (1.1–2.7)
Hypoglycemia	2.2%	0.18%	5.8 (2.4–14.3)
Hyperbilirubinemia	1.3%	0.1%	11.2 (3.6–34)
Admission to newborn intensive care unit	6.3%	2.5%	1.7 (1.1–2.7)
Hospitalization more than 4 days	10.5%	3.3%	2.6 (1.8–3.9)

Modified from Bates E, Rouse DJ, Mann ML, Chapman V, Carlo WA, Tita AT. Neonatal outcomes after demonstrated fetal lung maturity before 39 weeks of gestation. Obstet Gynecol 2010;116:1288–95.

Bates E, Rouse DJ, Mann ML, Chapman V, Carlo WA, Tita AT. Neonatal outcomes after demonstrated fetal lung maturity before 39 weeks of gestation. Obstet Gynecol 2010;116:1288–95.

Clark SL, Miller DD, Belfort MA, Dildy GA, Frye DK, Meyers JA. Neonatal and maternal outcomes associated with elective term delivery. Am J Obstet Gynecol 2009;200:156.e1–4.

Moore LE, Rayburn WF. Elective induction of labor. Clin Obstet Gynecol 2006;49:698–704.

Tita AT, Landon MB, Spong CY, Lai Y, Leveno KJ, Varner MW, et al. Timing of elective repeat cesarean delivery at term and neonatal outcome. Eunice Kennedy Shriver NICHD Maternal–Fetal Medicine Units Network. N Engl J Med 2009;360:111–20.

119

Prevention of recurrent preterm delivery

A 32-year-old woman, gravida 2, para 1, comes to your office for her second prenatal visit at 14 weeks of gestation. Her only prior pregnancy resulted in a spontaneous preterm birth at 28 weeks of gestation. She reports no vaginal bleeding, malodorous vaginal discharge, dysuria, or cramping. Examination reveals a long, firm, and closed cervix. The uterus is consistent with 14 weeks of gestation and the fetal heart rate is 140 beats per minute. You counsel her that the most effective approach to diminish her risk of recurrent preterm delivery is

(A) abstinence from sexual intercourse
* (B) administration of 17-α-hydroxyprogesterone caproate
(C) bed rest
(D) cervical cerclage placement based on history alone

Preterm birth, defined as birth before 37 weeks of gestation, is the leading cause of infant morbidity and mortality in the United States. Approximately 70–80% of preterm births occur spontaneously and a history of spontaneous preterm birth is a major risk factor for recurrence. The risk of recurrence is increased 1.5–2.0-fold for each preterm birth and another 1.5–2.0-fold for birth before 32 weeks of gestation. The patient described has a 27–48% risk of recurrent preterm birth without intervention.

Numerous therapeutic modalities for the prevention of preterm birth have been studied but few are supported by solid evidence. Weekly intramuscular administration of 17-α-hydroxyprogesterone caproate at 16 0/7–36 0/7 weeks of gestation in women with a singleton gestation and a prior spontaneous preterm birth at 20 0/7–36 6/7 weeks of gestation reduces the risk of recurrent preterm birth by approximately 35%. Administration of 17-α-hydroxyprogesterone caproate offers the best option for the described patient. Women with twins or triplets do not appear to benefit from prophylactic 17-α-hydroxyprogesterone caproate therapy. The mechanism by which 17-α-hydroxyprogesterone caproate reduces the rate of preterm birth is unknown, although an antiinflammatory effect has been postulated. Other interventions that reduce the risk of recurrent preterm birth include smoking cessation and screening and treatment of asymptomatic bacteriuria. Placement of a cervical cerclage also reduces the risk of preterm birth in women with a singleton pregnancy with a prior spontaneous preterm birth at less than 34 weeks of gestation and cervical length less than 25 mm before 24 0/7 weeks of gestation.

Sexual intercourse is not associated with an increased risk of preterm birth or recurrent preterm birth and, therefore, abstinence is not recommended. Insufficient evidence is available to support maternal activity restriction or bed rest. Furthermore, this strategy may increase the risk of thromboembolism and muscle deconditioning. Cerclage at 12 0/7–14 0/7 weeks of gestation in women with three or more prior preterm births with or without second-trimester losses may decrease the risk of recurrent preterm birth, but does not appear to be beneficial in women with fewer preterm births. Therefore, placement of a cerclage is not an appropriate option for the patient described.

Several other interventions have been studied but are either unproven or are supported by limited or conflicting evidence. In one randomized trial, daily administration of prophylactic vaginal progesterone was associated with a decreased rate of recurrent preterm delivery. However, a larger randomized trial in which the patients used daily vaginal progesterone gel showed no benefit. The use of other prophylactic tocolytic agents, such as prostaglandin inhibitors or oral beta-mimetics, does not appear to prevent preterm birth. Antibiotic treatment of women with bacterial vaginosis and a prior preterm birth has not consistently resulted in pregnancy prolongation. Therefore, these interventions are not recommended as routine care in the management of women at risk of recurrent preterm birth.

da Fonseca EB, Bittar RE, Carvalho MB, Zugaib M. Prophylactic administration of progesterone by vaginal suppository to reduce the incidence of spontaneous preterm birth in women at increased risk: A randomized placebo-controlled double-blind study. Am J Obstet Gynecol 2003;188:419–24.

Iams JD, Berghella V. Care for women with prior preterm birth. Am J Obstet Gynecol Am J Obstet Gynecol 2010;203:89–100.

Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. N Engl J Med 2003;348:2379–85.

O'Brien JM, Adair CD, Lewis DF, Hall DR, Defranco EA, Fusey S. Progesterone vaginal gel for the reduction of recurrent preterm birth: primary results from a randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2007;30:687–96.

Sosa C, Althabe F, Belizán J, Bergel E. Bed rest in singleton pregnancies for preventing preterm birth. Cochrane Database Syst Rev 2004;(1):CD003581.

Yost NP, Owen J, Berghella V, Thom E, Swain M, Dildy GA, et al. Effect of coitus on recurrent preterm birth. Obstet Gynecol 2006;107:793–7.

120

Use of biophysical profile in pregnancy management

A 39-year-old woman, gravida 2, para 0, at 36 weeks of gestation has type 1 diabetes mellitus and chronic hypertension. She is undergoing antepartum fetal assessment with biophysical profile (BPP) testing. After 75 minutes, she has a BPP of 2/10 and an amniotic fluid index of 2 cm. The best next step in management is to

(A) repeat BPP in 24 hours
(B) perform contraction stress test
(C) perform vibroacoustic stimulation
* (D) proceed to delivery

Biophysical profile scoring involves assessment by means of a nonstress test plus four ultrasonographic parameters: 1) evaluation of fetal tone, 2) movement, 3) breathing, and 4) amniotic fluid volume. Each parameter is given a score of two if considered normal or present, and zero if abnormal or absent (Table 120-1). A total score of 10/10 is strongly associated with normal acid–base status and the predicted perinatal morality within 1 week is less than 1 per 1,000. With decreasing score, there is increased risk of fetal compromise and higher risk of perinatal mortality (Table 120-2).

Because of the lower sensitivity of certain central nervous system autonomic control centers with progressive fetal hypoxia, nonstress testing and fetal breathing movements become abnormal before loss of fetal movements and tone. Except in cases of significant hyperglycemia, the presence of fetal breathing movements are indicative of normal acid–base status. In a woman with poorly controlled diabetes mellitus, hyperglycemia can artificially induce fetal breathing movements even when there is significant hypoxia–acidemia. Another biophysical profile scoring parameter that can be falsely reassuring in pregnancies in women who have diabetes mellitus is amniotic fluid volume, which may be increased (eg, polyhydramnios) even in a patient with uteroplacental insufficiency.

Although other biophysical profile scoring parameters are more indicative of the acute fetal state, decreased amniotic fluid volume is often a sign of chronic fetal compromise. Decreased amniotic fluid volume is associated with decreased fetal renal perfusion and is reflective of uteroplacental insufficiency.

Biophysical profile scores between 0 and 4 are interpreted to reflect acute fetal compromise and warrant immediate evaluation and possible delivery, depending on gestational age and maternal condition. A score of 2 with absence of fetal breathing, movement, and tone should prompt consideration for maternal stabilization and immediate delivery. Depending on which parameters are abnormal, a BPP of 6 may be repeated in 24 hours.

TABLE 120-1. Criteria for Biophysical Profile Scoring

Variable	Normal or Present Behavior (Score = 2)	Abnormal, Absent, or Insufficient Behavior (Score = 0)
Fetal breathing movements	One or more episodes of 30-second duration, within 30 minutes	Completely absent breathing or no sustained episodes
Body or limb movements	Three or more discrete body movements in 30 minutes	Less than three body or limb movements in a 30-minute observation period
Fetal tone–posture	Demonstration of active extension with rapid return to flexion of fetal limbs or opening and closing of hand	Low-velocity movement only. Incomplete flexion, flaccid extremity positions, abnormal fetal posture
Nonstress test	Two or more episodes of fetal heart rate accelerations within 20 minutes	Nonreactive test
Amniotic fluid evaluation	At least one pocket greater than 2 cm with no umbilical cord	No cord-free pocket greater than 2 cm

Adapted from Manning FA. Fetal biophysical profile. Obstet Gynecol North Am 1999;26:557–77. Copyright 1999 by Elsevier.

TABLE 120-2. Systematic Application of Biophysical Profile Scoring

Biophysical Profile Scoring	Interpretation	Predicted Perinatal Mortality/1,000*	Recommended Management
10/10 8/8 8/10 (AFV normal)	No evidence of fetal asphyxia present.	Less than 1/1,000	No acute intervention on fetal basis. Serial testing indicated by disorder-specific protocols.
8/10 (oligohydramnios)	Chronic fetal compromise likely (unless ROM is proven).	89/1,000	For absolute oligohydramnios, prove normal urinary tract, disprove undiagnosed ROM, consider antenatal steroids, then deliver.
6/10 (AFV normal)	Equivocal test, fetal asphyxia is not excluded.	Depends on progression; average of 61/1,000	Repeat testing immediately, before assigning final value. If score is 6/10, then 10/10, in two continuous 30-minute periods, manage as 10/10. For persistent 6/10, deliver the mature fetus, repeat within 24 hours in the immature fetus, then deliver if less than 6/10.
4/10	Acute fetal asphyxia likely. If AFV–oligohydramnios, acute on chronic asphyxia very likely.	91/1,000	Deliver by obstetrically appropriate method, with continuous monitoring.
2/10	Acute fetal asphyxia, most likely with chronic decompensation.	125/1,000	Deliver for fetal indications (usually cesarean delivery).
0/10	Severe, acute asphyxia virtually certain.	600/1,000	If fetal status is viable, deliver immediately by cesarean delivery.

Abbreviations: AFV, amniotic fluid volume; ROM, rupture of membranes.

*Per test, within 1 week of the result shown, if no intervention. For scores of 0, 2, or 4, intervention should begin virtually immediately, provided the fetus is viable. For all interventions, lethal anomaly should be excluded as a potential cause of the abnormal behavior.

Manning FA. Fetal biophysical profile. Obstet Gynecol North Am 1999;26:557–77. Copyright 1999 by Elsevier.

For a BPP of 8 or 10, repeat testing in 1 week is usually reasonable.

In this case, given the advanced gestational age, the best option is delivery. Repeating a biophysical profile in 24 hours would not be appropriate because of the possibility of fetal death. In this case, performing additional types of antepartum testing (vibroacoustic stimulation, contraction stress test) is not advisable given the ominous BPP results.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. ACOG Practice Bulletin 9. Washington, DC: ACOG; 1999.

Creasy R, Resnik R, Iams J, Lockwood C, Moore T, Greene M. Creasy and Resnik's maternal–fetal medicine: principles and practice. 6th ed. Philadelphia (PA): Saunders Elsevier; 2009. p. 364–9.

Dayal AK, Manning FA, Berck DJ, Mussalli GM, Avila C, Harman CR, et al. Fetal death after normal biophysical profile score: An eighteen–year experience. Am J Obstet Gynecol 1999;181:1231–6.

Manning FA. Antepartum fetal testing: a critical appraisal. Curr Opin Obstet Gynecol 2009;21:348–52.

Manning FA, Morrison I, Harman CR, Menticoglou SM. The abnormal fetal biophysical profile score. V. Predictive accuracy according to score composition. Am J Obstet Gynecol 1990;162:918–24; discussion 924–7.

121

Diabetes mellitus

A 25-year-old nulligravid woman comes to your office for a preconception care visit. She has been diagnosed with type 2 diabetes mellitus for the past 3 years. With diet, exercise, and weight loss, she was able to improve her glucose control and discontinue her oral hypoglycemic agent. She wishes to avoid going back on medication if she becomes pregnant. You counsel her that because of physiologic changes in her pregnancy, her glucose tolerance may worsen as the pregnancy advances. The placental protein most closely associated with postprandial elevations of maternal glucose in the third trimester is

(A) glucose transporter 1 protein
* (B) human placental lactogen
(C) inhibin
(D) human chorionic gonadotropin
(E) activin

Normal pregnancy physiologic carbohydrate metabolism insures the consistent delivery of glucose to the fetus. Some physiologic differences exist in the body's assimilation of carbohydrate intake from early pregnancy to late pregnancy (Table 121-1). Early pregnancy is characterized by enhanced glucose metabolism due to placental glucose transport and increased insulin secretory capacity. In later pregnancy, fasting hypoglycemia and hyperinsulinemia are still found but postprandial hyperglycemia, elevated free fatty acids, and increased tissue resistance to insulin are found as well.

The placenta demonstrates facilitated transport of glucose from the maternal circulation to the fetal circulation mediated by sodium-independent transporter proteins, such as glucose transporter 1. Placental hormones, including estrogen, progesterone, and human placental lactogen, cause islet beta cell hypertrophy that leads to increased insulin secretory capacity in healthy pregnant women. In normal pregnancy, this leads to a normal mild fasting hypoglycemia.

TABLE 121-1. Selected Physiologic Changes in Pregnancy and Effect on Glucose Metabolism

Physiologic Change in Pregnancy	Effect on Glucose Metabolism
Elevated human placental lactogen	Antagonizes insulin action Increases free fatty acids
Placental glucose transporter	Lowers maternal fasting blood sugar
Islet cell hypertrophy	Increased insulin secretory capacity
Elevated leptin levels	Role is unclear but elevated levels found in diabetic pregnancy
Placental insulinases	Unlikely to affect levels of circulating maternal insulin

As pregnancy progresses, human placental lactogen and human placental growth hormone increase lipolysis. Normal women can quickly switch to fatty acid metabolism for their energy needs, preserving glucose as a fuel for the fetus and the maternal central nervous system. Norbert Freinkel classically referred to this phenomenon as "accelerated starvation of pregnancy." Later pregnancy is a state of insulin resistance. Postreceptor mechanisms after insulin binding may cause disruption in insulin signaling in maternal striated muscle cells. A 50% decrease in insulin sensitivity occurs in late pregnancy. Human placental growth hormone, cortisol, and tumor necrosis factor-alpha contribute to postreceptor insulin resistance. Elevated leptin levels and decreased adiponectin levels also may play a role in insulin resistance. In normal pregnancy, islet cell secretory capacity can maintain glucose homeostasis despite this insulin resistance. Although placental insulinases have been identified that degrade maternal insulin, this is not thought to greatly affect maternal glucose metabolism. Therefore, postprandial glucose and insulin levels in the third trimester are higher than in the nonpregnant state and higher than in early pregnancy.

The normal pregnancy changes in glucose metabolism are thought to unmask underlying islet cell defects that contribute to type 2 diabetes mellitus and lead to gestational diabetes mellitus. Potential limitations to insulin secretion include incomplete autoimmune destruction of islet mass, genetic causes for decreased islet mass and function occurring in an individual with chronic insulin resistance. In women with preexisting type 2 diabetes mellitus, these pathophysiologic changes may exaggerate their pregnancy physiology and result in hyperglycemia.

Inhibin, human chorionic gonadotropin, and activin do not have an appreciable effect on maternal glucose levels.

Buchanan TA, Xiang AH. Gestational diabetes mellitus. J Clin Invest 2005;115:485–91.

Gestational diabetes. ACOG Practice Bulletin No. 30. American College of Obstetricians and Gynecologists. Obstet Gynecol 2001;98:525–38.

Metzger BE, Buchanan TA, Coustan DR, de Leiva A, Dunger DB, Hadden DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus [published erratum appears in Diabetes Care 2007;30:3154]. Diabetes Care 2007;30(suppl 2):S251–60.

Phelps RL, Metzger BE, Freinkel N. Carbohydrate metabolism in pregnancy. XVII. Diurnal profiles of plasma glucose, insulin, free fatty acids, triglycerides, cholesterol, and individual amino acids in late normal pregnancy. Am J Obstet Gynecol 1981;140:730–6.

122

Cerebral palsy

A 24-year-old woman, gravida 2, para 0, at 26 weeks of gestation comes to the hospital with her second episode of preterm labor. She received antenatal steroids and had a negative culture for group B streptococci (GBS) 5 days earlier. Monitoring reveals uterine contractions every 3 minutes with a Category I fetal heart rate tracing. Her cervix is 6 cm dilated and 100% effaced, and the fetal head is at 0 station. The best next step in management is to administer

(A) a rescue course of antenatal corticosteroids
* (B) magnesium sulfate
(C) antibiotics for GBS prophylaxis
(D) indomethacin

Cerebral palsy is characterized by abnormal control of movement and posture that results in activity limitation and is caused by nonprogressive damage or dysfunction of the developing fetal or infant brain. Preterm birth is a major risk factor for cerebral palsy and the risk increases with decreasing gestational age. Births before 34 weeks of gestation account for 17–32% of all cases of cerebral palsy.

Data from randomized trials suggest that administration of magnesium sulfate before early preterm birth reduces the risk of cerebral palsy in surviving infants by 32%. Therefore, magnesium sulfate would be the recommended option in the described patient. Reduced vascular instability, prevention of hypoxic injury, and inhibition of cytokine or excitatory amino acid damage are some of the possible mechanisms to explain this protective association. The American College of Obstetricians and Gynecologists recommends that health care providers who prescribe magnesium sulfate for fetal neuroprotection should develop guidelines in accordance with one of the trials listed in Appendix F.

Antenatal steroids have many beneficial effects including a reduced rate of cerebral palsy in neonates born at 24–30 weeks of gestation. The American College of Obstetricians and Gynecologists has stated that a single rescue course of antenatal corticosteroids may be considered if the antecedent treatment is given more than 2 weeks prior, if the gestational age is less than 32 6/7 weeks, and if the woman is likely to give birth within the next week. A rescue course of antenatal corticosteroids is not an appropriate choice because the described patient does not meet these criteria.

Chorioamnionitis is a recognized risk factor for cerebral palsy in term and preterm neonates and GBS colonization is associated with an increased risk of chorioamnionitis. Antibiotics are not indicated for GBS prophylaxis if a culture was negative for GBS within the preceding 5 weeks, which is the case in this patient.

Use of a tocolytic may prolong pregnancy for 2–7 days, allowing for the administration of antenatal steroids and maternal transport to a facility with a neonatal intensive care unit. Tocolytics are likely to be less effective in women with advanced cervical dilation. Given that the described patient has a cervix that is 6 cm dilated and that she recently received antenatal steroids, the use of indomethacin would not be the best option for her. Although magnesium sulfate may function as a tocolytic agent, the primary reason to initiate this medication is to minimize the risk of cerebral palsy.

American College of Obstetricians and Gynecologists. Antenatal corticosteroid therapy for fetal maturation. Committee Opinion No. 475. Obstet Gynecol 2011;117:422–4.

Antenatal corticosteroid therapy for fetal maturation. Committee Opinion No. 475. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:422–4.

Crowther CA, Hiller JE, Doyle LW, Haslam RR. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. Australasian Collaborative Trial of Magnesium Sulphate (ACTOMg SO4) Collaborative Group. JAMA 2003;290:2669–76.

Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD004661. DOI: 10.1002/14651858.CD004661.pub3; 10.1002/14651858.CD004661.pub3.

Magnesium sulfate before anticipated preterm birth for neuroprotection. Committee Opinion No. 455. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;115:669–71.

Marret S, Marpeau L, Zupan-Simunek V, Eurin D, Leveque C, Hellot MF, et al. Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial*. PREMAG trial group. BJOG 2007;114:310–8.

Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. Eunice Kennedy Shriver NICHD Maternal–Fetal Medicine Units Network. N Engl J Med 2008;359:895–905.

Vincer MJ, Allen AC, Joseph KS, Stinson DA, Scott H, Wood E. Increasing prevalence of cerebral palsy among very preterm infants: a population-based study. Pediatrics 2006;118:e1621–6.

123

Fetal death

A 21-year-old healthy woman, gravida 2, para 1, comes to the labor and delivery unit at 36 weeks of gestation with absent fetal heart tones, and is diagnosed with antepartum fetal death. Her obstetric history includes a prior low segment cesarean delivery because of nonreassuring fetal heart tones. Ultrasonography and clinical examination confirm estimated fetal weight of 2,900 g with complete breech presentation. On pelvic examination, her cervix is 1 cm dilated, 50% effaced, posterior position, and firm. Her laboratory results show normal platelet count and no evidence of disseminated intravascular coagulation. She wants delivery as soon as possible. The best delivery management for this patient is

(A) labor induction with misoprostol
(B) labor induction with prostaglandin E_2
* (C) labor induction with transcervical Foley catheter
(D) cesarean delivery without labor

Delivery options for women with a prior cesarean delivery who develop antepartum fetal death in the third trimester are often limited. Given the lack of fetal benefit of cesarean delivery and the known maternal risks of cesarean delivery, vaginal delivery is the preferred route in almost all cases. Thus, a complete breech presentation is not a contraindication to attempting trial of labor after cesarean delivery (TOLAC), even if labor induction is required. The challenging aspect regarding intrapartum management of these women is when the patient is not in labor and does not have a favorable cervix, as in the described case.

Given the association of uterine rupture with prostaglandin E_2 and misoprostol in women with prior cesarean delivery, these agents for cervical ripening and labor induction are not the preferred choices. Despite the lack of fetal harm if uterine rupture would develop with a TOLAC, maternal morbidity, such as hemorrhage, need for transfusion, and need for hysterectomy all exist. In women with a prior cesarean delivery who develop third-trimester stillbirth and require cervical ripening with a Foley catheter, the risk of uterine rupture is similar to women in spontaneous labor. Therefore, TOLAC often is encouraged in these cases, and may even be an option in women with multiple cesarean deliveries or those who have experienced one prior classical cesarean delivery.

In a multicenter observational study of 209 women who had an antepartum stillbirth after 24 weeks of gestation and who underwent TOLAC, the vaginal delivery success rate was 86.7%; uterine rupture occurred in five women (2.9%). Most women in this cohort had labor induction or augmentation (83.3%). Among the women whose delivery was induced, the rate of uterine rupture was 3.4%, but none of these women required hysterectomy. If cesarean delivery without a labor attempt is performed, morbidity may be higher because of greater risk of hemorrhage. In the described case, although there is concern for fetal head entrapment, labor induction may be attempted.

Guise JM, Eden K, Emeis C, Denman MA, Marshall N, Fu RR, et al. Vaginal birth after cesarean: new insights. Evid Rep Technol Assess (Full Rep) 2010;(191):1–397.

Ramirez MM, Gilbert S, Landon MB, Rouse DJ, Spong CY, Varner MW, et al. Mode of delivery in women with antepartum fetal death and prior cesarean delivery. Am J Perinatol 2010;27:825–30.

Vaginal birth after previous cesarean delivery. Practice Bulletin No. 115. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:450–63.

124

Cardiovascular physiology

A 35-year-old woman, gravida 1, comes to your office for prenatal care at 10 weeks of gestation. She tells you that she has fatigue and an inability to climb steps without stopping. Chest examination reveals a soft diastolic murmur best heard at the apex. Echocardiography demonstrates mitral stenosis and normal sinus rhythm. Her atria are normal in size, and left and right ventricular contractility appears normal. Her family physician expresses concern about her cardiac ability to tolerate pregnancy. The physiologic change of pregnancy that will most negatively affect her cardiac function with mitral stenosis is

* (A) increase in total blood volume
(B) third trimester plateau of cardiac output
(C) levorotation of the heart
(D) decrease in cardiac afterload

Management of pregnant women with cardiac disease is aided by knowledge of the physiologic changes that occur in pregnancy. Cardiovascular changes in pregnancy begin early. With pregnancy, relaxation of the vasculature is probably mediated by changes in the nitric oxide and prostacyclin–thromboxane systems. The placental circulation likely serves to decrease the vascular resistance. The systemic vascular resistance is lowest in the second trimester and then returns to normal at term. Additionally, there are changes in the renin–angiotensin system. In the kidney, this vasodilation leads to fluid retention. Total blood volume increases 40–50% during pregnancy. A corresponding increase occurs in maternal cardiac output that plateaus later in the third trimester. The cardiac output increases because of increased preload with blood volume expansion, increased stroke volume, decreased afterload due to drops in systemic vascular resistance, and a 10–20% linear increase in the maternal heart rate (see Table 124-1). Many normal symptoms of pregnancy, such as shortness of breath, fatigue, and increasing heart rate, are similar to signs of cardiac decompensation making the diagnosis of worsening cardiac function challenging.

In labor, cardiac output is further increased because of intermittent autotransfusions from the contracting uterus, the work of labor, and pain and anxiety in the mother. Cardiac output reaches its peak shortly after delivery then decreases to third-trimester values over the hours after delivery. Hemodynamic changes return to baseline 2–4 weeks later with the cardiovascular system back to nonpregnant parameters by 6–12 weeks.

As one of the most commonly identified cardiac lesions, mitral stenosis may first become symptomatic in pregnancy because of difficulty handling the increased circulating blood volume. Pulmonary edema, right-sided heart failure, and atrial fibrillation from a dilated right atrium can all be presenting symptoms in a pregnant woman with mitral stenosis primarily due to increased blood volume.

TABLE 124-1. Summary of Hemodynamic Changes of Pregnancy

Hemodynamic Alteration	Time of Peak Effect	Potential Risks
Cardiac output increases 30–50%	20–24 weeks	Women with limited cardiac function or reserve may develop congestive heart failure
Stroke volume increases 20%	20–24 weeks	Increased preload is a problem for obstructive lesions (mitral or aortic stenosis) or ventricular dysfunction
Heart rate increases 10–20%	Third trimester	Tachycardia causes palpitations and impairs ventricular filling
Blood volume increases 40%	20–24 weeks	Physiologic anemia of pregnancy
Peripheral vasodilation	Throughout	Decreased blood pressure; decreased valvular regurgitation
Minute ventilation	Second trimester	Sensation of tachypnea or dyspnea

Mendelson MA. Pregnancy in the woman with preexisting cardiovascular disease. In: Global library for women's medicine. London: Foundation for the Global Library for Women's Medicine; 2008. (ISSN: 1756-2228); DOI 10.3843/GLOWM.10161. Available at: http://www.glowm.com/?p=glowm.cml/section_view&articleid=161. Retrieved June 11, 2012.

The plateau of cardiac output in the third trimester allows patients with mitral stenosis to remain relatively stable throughout this period. The decrease in cardiac afterload during pregnancy may benefit patients with left-sided valvular lesions. Although increase in baseline heart rate may negatively affect cardiac function, the increase in total blood volume is a more clinically important factor. Although levorotation of the heart does occur in pregnancy it does not negatively affect the cardiac function in a patient with mitral stenosis.

Carbillon L, Uzan M, Uzan S. Pregnancy, vascular tone, and maternal hemodynamics: a crucial adaptation. Obstet Gynecol Surv 2000; 55:574–81.

Carlin A, Alfirevic Z. Physiological changes of pregnancy and monitoring. Best Pract Res Clin Obstet Gynaecol 2008;22:801–23.

Mendelson MA. Pregnancy in the woman with preexisting cardiovascular disease. In: Global library for women's medicine. London: Foundation for the Global Library for Women's Medicine; 2008. Available at: http://www.glowm.com/?p=glowm.cml/section_view&articleid=161. Retrieved June 11, 2012.

Moghbeli N, Pare E, Webb G. Practical assessment of maternal cardiovascular risk in pregnancy. Congenit Heart Dis 2008;3:308–16.

Reimold SC, Rutherford JD. Clinical practice. Valvular heart disease in pregnancy. N Engl J Med 2003;349:52–9.

125

Cystic fibrosis

A 27-year-old white woman, gravida 1, comes to your office for her first prenatal visit. The patient and the father of the baby have no family members with cystic fibrosis. She desires screening for cystic fibrosis. Her cystic fibrosis screen result is negative for 32 mutations. You counsel her that the risk of cystic fibrosis to her fetus is

(A) increased
* (B) decreased
(C) indeterminate
(D) zero

Cystic fibrosis is an autosomal recessive disease caused by a mutation in the cystic fibrosis transmembrane regulator gene. More than 1,000 mutations have been identified in this gene. The most common mutation in the population is Δ*F508*. Although other mutations, such as *W1282X*, *G542X*, and *G551D*, occur relatively frequently, most mutations are found in less than 0.1% of the population.

The clinical phenotype of cystic fibrosis is highly variable and imprecisely related to the genotype. Cystic fibrosis is a progressive multisystem disease that primarily affects the pulmonary system and digestive system. Affected individuals produce viscous mucous. The mucous builds up and can cause obstruction in the lungs and pancreas. Recurrent infection or persistent pulmonary infection and pancreatic insufficiency are common. The primary treatment for cystic fibrosis is supportive and consists of clearance of mucous in the lungs, aggressive treatment of pulmonary infection, and nutritional support. Life expectancy is significantly reduced, and median survival is in the mid-30s.

The overall incidence of cystic fibrosis is dependent on the ethnic and geographic distribution of the population. The highest incidence is in non-Hispanic whites and Ashkenazi Jews, and the lowest incidence is in Asian Americans (Table 125-1). The sensitivity of the screening test is dependent on the frequency of the carrier rate in the population before screening. The more frequent the carrier rate, the better the screening test performs. The carrier rate before and after testing is shown in Table 125-1. The risk for the individual to be a carrier of cystic fibrosis is significantly decreased but is not eliminated by a negative screening test.

The American College of Obstetricians and Gynecologists and the American College of Medical Genetics have jointly endorsed guidelines for cystic fibrosis screening. According to the guidelines, screening is recommended for all patients who seek preconception counseling or prenatal care regardless of ethnicity or risk factors. Screening the patient first is usually the most cost-effective and practical method. The father of the baby should be screened

TABLE 125-1. Cystic Fibrosis Detection and Carrier Rates Before and After Testing

Ethnic Group	Detection Rate (%)	Carrier Rate Before Testing	Approximate Carrier Rate After Negative Testing
Ashkenazi Jewish	94	1/24	1/380
Non-Hispanic white	88	1/25	1/200
Hispanic white	72	1/58	1/200
African American	64	1/61	1/170
Asian American	49	1/94	1/180

Update on carrier screening for cystic fibrosis. Committee Opinion No. 486. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:1028–31.

only if the patient is a carrier. The goal of carrier screening is to identify couples at risk of having a child with cystic fibrosis.

Ultrasonography is not considered a screening tool for cystic fibrosis but echogenic bowel has been associated with cystic fibrosis. If echogenic bowel is seen on screening ultrasonography, the risk of cystic fibrosis is approximately 3%, however, ranges of 0–8% have been reported. Of fetuses with cystic fibrosis, 10–20% will have echogenic bowel. Echogenic bowel may be an early sign of a meconium ileus.

Castellani C, Picci L, Tamanini A, Girardi P, Rizzotti P, Assael BM. Association between carrier screening and incidence of cystic fibrosis. JAMA 2009;302:2573–9.

Haddow JE, Palomaki GE. Population based prenatal screening for cystic fibrosis via carrier testing. ACCE review. Atlanta (GA): Centers for Disease Control and Prevention; 2002. Available at: http://www.cdc.gov/genomics/gtesting/ACCE/ACCE.htm. Retrieved June 4, 2012.

Norton ME. Genetic screening and counseling. Curr Opin Obstet Gynecol 2008;20:157–63.

Scotet V, Dugueperoux I, Audrezet MP, Audebert-Bellanger S, Muller M, Blayau M, et al. Focus on cystic fibrosis and other disorders evidenced in fetuses with sonographic finding of echogenic bowel: 16-year report from Brittany, France. Am J Obstet Gynecol 2010;203:592.e1–6.

Update on carrier screening for cystic fibrosis. Committee Opinion No. 486. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:1028–31.

126

Congenital cytomegalovirus in pregnancy

A 24-year-old woman, gravida 1, at 8 weeks of gestation is a registered nurse who has recently begun employment in a pediatrics unit. She expresses concern over her risk of contracting cytomegalovirus (CMV). The best strategy to prevent her from contracting CMV infection is

(A) ganciclovir prophylaxis
* (B) universal precautions including good hand washing
(C) transfer to adult medicine unit
(D) hyperimmune globulin if she develops a mononucleosis-like illness

In an adult, primary infection with CMV occurs from close contact of an uninfected person with an infected person's secretions. Approximately 30–50% of reproductive-aged women in the United States are susceptible to new CMV infection. Seroconversion, indicating primary infection, occurs in 1–4% of seronegative pregnancies. After a primary infection, there exists a 30–40% risk of transmission to the fetus. Similar to other members of the herpes virus family, CMV has the ability to become latent and then be reactivated. This is known as secondary infection and carries a lesser risk of fetal transmission (1%). Approximately 0.7% of newborns in the United States are estimated to have congenital CMV infection. Postnatal clinical manifestations of in utero CMV vary widely from severely affected to asymptomatic (90%). Congenital CMV accounts for 20% of sensorineural hearing loss and also has been associated with fetal growth restriction, microcephaly, hepatosplenomegaly, chorioretinitis, jaundice, blindness, and psychomotor delay. See Figure 126-1 for characteristics of CMV infection in pregnancy.

Most maternal infections go unnoticed, although maternal symptoms of illness may on occasion lead to documentation of CMV seroconversion (negative immunoglobulin G [IgG] antibody to CMV to positive immunoglobulin M in early infection followed by IgG). Early IgG antibody against CMV binds less tightly to a virus with low avidity, followed by a higher avidity antibody after 3–4 months. The finding of low (less than 30%) CMV IgG avidity may help identify infections of less than 3 months duration and suggest primary infection. Fetal ultrasonographic findings in congenital CMV infections include growth restriction, cerebral ventriculomegaly, echogenic bowel, liver calcifications, microcephaly, and hydrops. These findings overlap with other conditions and are not diagnostic of CMV infection. Amniotic

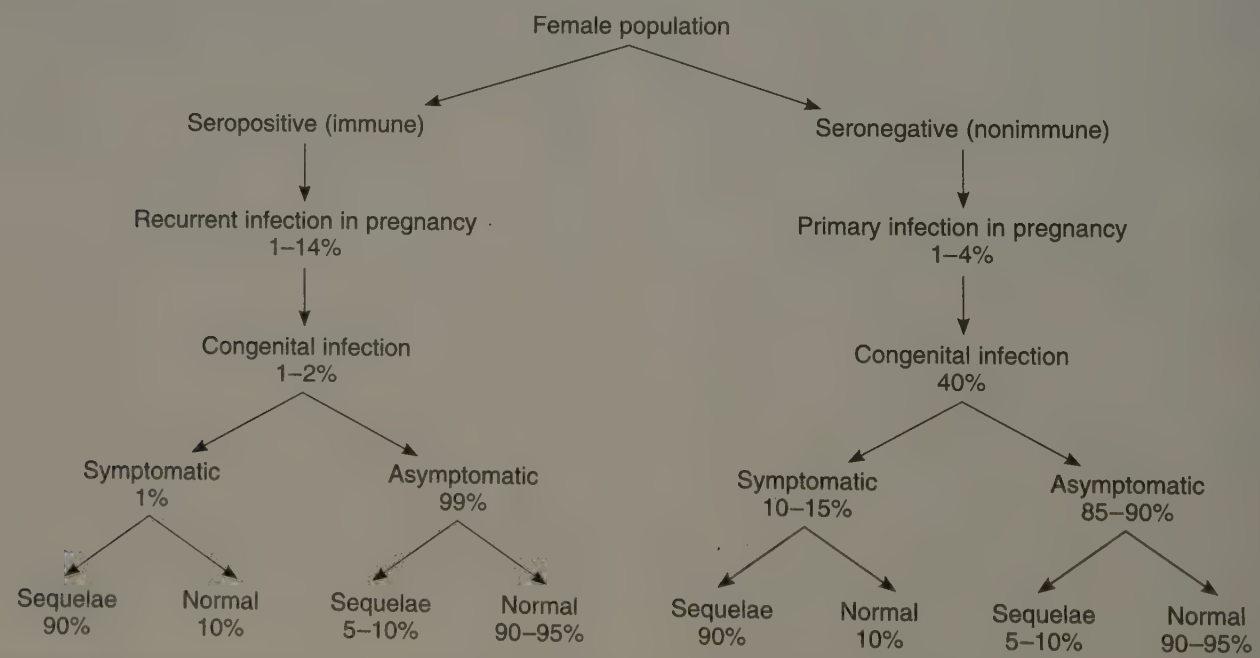


FIG. 126-1. Characteristics of cytomegalovirus infection in pregnancy.

fluid polymerase chain reaction for CMV is a widely used in utero diagnostic test. Amniotic fluid culture and cord blood sampling for immunoglobulin M also may be used. Case series of fetal treatment with CMV hyperimmune globulin and ganciclovir demonstrate potential benefit, however, the data are insufficient to recommend such treatment outside of trials. The long-term outcome for the fetus with CMV infection is difficult to predict. Congenital CMV infection is diagnosed in the newborn with detection of virus in the urine, blood, or saliva in the first 2–3 weeks of life.

Routine screening of pregnant women for CMV serostatus is not recommended because past infection is not protective and experience with treatment of in utero infection is limited. Although limited trials of potential CMV vaccines for prevention of infection have been undertaken, no current vaccines are available for widespread use. Young children in day care frequently are infected with CMV. Therefore, recommendations for prevention center on careful hygiene during the care of toddlers as the best preventive strategy. Health care workers experience CMV seroconversion at the same rate as the general population. Standard universal precautions for patient contact, including good hand washing, are recommended for individuals with occupational exposure to CMV. Therefore, requesting a transfer to the adult medical ward also would not be helpful.

Amir J, Wolf DG, Levy I. Treatment of symptomatic congenital cytomegalovirus infection with intravenous ganciclovir followed by long-term oral valganciclovir. Eur J Pediatr 2010;169:1061–7.

Cannon MJ. Congenital cytomegalovirus (CMV) epidemiology and awareness. J Clin Virol 2009;46 Suppl 4:S6–10.

Fowler KB, Pass RF. Risk factors for congenital cytomegalovirus infection in the offspring of young women: exposure to young children and recent onset of sexual activity. Pediatrics 2006;118:e286–92.

Gardella C. Cytomegalovirus in pregnancy. In: Global library for women's medicine. London: Foundation for the Global Library for Women's Medicine; 2008. Available at: http://www.glowm.com/?p=glowm.cml/section_view&articleid=182. Retrieved June 11, 2012.

Moise KJ, Wolfe H. Treatment of second trimester fetal cytomegalovirus infection with maternal hyperimmune globulin. Prenat Diagn 2008;28:264–5.

Stagno S, Whitley RJ. Herpesvirus infections of pregnancy. Part I: Cytomegalovirus and Epstein-Barr virus infections. N Engl J Med 1985;313:1270–4.

Yinon Y, Farine D, Yudin MH. Screening, diagnosis, and management of cytomegalovirus infection in pregnancy. Obstet Gynecol Surv 2010;65:736–43.

127
Migraine

A 34-year-old woman at 6 weeks of gestation seeks treatment for her daily headaches. She has a history of severe asthma since childhood and migraine headaches since age 16 years. The headaches are severe, unilateral, last 8–10 hours, and interfere with her daily functioning. Before pregnancy, she had been taking daily ibuprofen but has switched to daily acetaminophen during pregnancy. The best pharmacotherapy for prevention of recurrent migraine headache for this patient is

(A) codeine
(B) ibuprofen
* (C) nifedipine
(D) propranalol
(E) phenylephrine

Most patients with migraines are women in their childbearing years. The need for treatment of migraine in pregnancy is commonly encountered by the obstetrician–gynecologist. Treatment in pregnancy is complicated by the potential for teratogenic and other adverse effects on the developing fetus. In all recommendations about pharmacologic therapy, the risk–benefit ratio must be considered. Women should be given information to make an informed decision.

In the treatment of acute migraine, nonpharmacologic measures should be initially considered. Rest, reassurance, and ice packs may be helpful. Acupuncture and biofeedback also have been employed in pregnancy. If medications are needed, acetaminophen alone, or acetaminophen with codeine, or codeine alone have been used as first-line agents because of their long history of relative safety in pregnancy. Use of nonsteroidal antiinflammatory agents should be limited to very short courses in pregnancy, especially in the third trimester because of the risk of premature closure of ductus arteriosus in the fetus. The triptans are generally not recommended as first-line therapy but can be used in certain circumstances. Ergotamine and dihydroergotamine are contraindicated in pregnancy because of the potential for uterotonic effects. For severe migraine with nausea and vomiting, intravenous hydration and treatment with antiemetics are indicated. Diphenhydramine and metoclopramide generally are considered safe to use in pregnancy.

Prevention of migraines centers on lifestyle changes and avoidance of triggers. Recommendations include development of regular sleeping and eating patterns, regular exercise, and cessation of smoking if applicable. For certain individuals, triggers should also be avoided, such as ingestion of red wine (not recommended in pregnancy), monosodium glutamate, and tyramine.

When migraines are frequent and not controlled by lifestyle changes, daily prophylactic medication for migraine should be considered. Indications for pharmacologic preventive therapy for migraine include the following:

- Frequency greater than one headache per week
- Failure or overuse of acute medication
- Adverse effects of acute treatment
- Patient preference
- Headaches that interfere with daily function despite acute treatment

Medications for migraine prevention include β-adrenergic blockers, antidepressants, tricyclic and selective serotonin reuptake inhibitors, calcium channel blockers, serotonin antagonists, anticonvulsants, and nonsteroidal antiinflammatory agents. In pregnancy, β-blockers, calcium channel blockers (such as nifedipine), and antidepressants are most commonly employed. The lowest effective dose should be used. A full trial of preventive therapy requires 2–6 months of treatment. In many cases, preventive therapy is stopped prematurely. In selecting a medication, the health care provider should consider any coexisting medical conditions that the patient may have. For example, if the patient has hypertension, a β-blocker or calcium channel blocker may be most appropriate. If depression is present, a selective serotonin reuptake inhibitor may be a good choice.

The patient described has severe daily headaches that interfere with her functioning. She is a good candidate for preventive therapy. Propranolol is not the best choice given her history of severe asthma. Codeine is used for acute treatment and could be added to her acute treatment regime, but it is not a good choice for chronic use. Ibuprofen also is used for acute treatment, however, its use is limited in pregnancy to short duration and it should be avoided in later pregnancy. Phenylephrine is not a treatment for migraine, although it may be useful for sinus headache. Of the choices listed, nifedipine would offer

the best pharmacotherapy for prevention of headache for this patient.

Goadsby PJ. Pathophysiology of migraine. Neurol Clin 2009;27:335–60.

Lay CL, Broner SW. Migraine in women. Neurol Clin 2009;27:503–11.

Silberstein SD. Migraine and other headache disorders. Clin Updates Womens Health 2009;VIII (5):1–56.

128

External cephalic version

A 37-year-old woman, para 1, at 35 weeks of gestation is found to have a breech presentation. She had a prior low transverse cesarean delivery 1 year ago for preeclampsia and failed induction of labor. Her past medical history is remarkable only for mild intermittent asthma. On ultrasonographic evaluation, the placenta is anterior. The amniotic fluid index is 10 cm. The fetus has an estimated weight of 2,600 g, and no anomalies are detected. The patient requests that you perform an external cephalic version today because of her work schedule. You tell her that you do not recommend the procedure because of her

* (A) gestational age
(B) placental location
(C) amniotic fluid index
(D) prior cesarean delivery

Approximately 3–4% of fetuses at term are in breech presentation with most being delivered by cesarean delivery. The goal of an external cephalic version is to increase term vaginal deliveries. In choosing to offer this method of delivery, the benefits, risks, and likelihood of success need to be considered.

External cephalic version is considered a relatively safe procedure that is successful in approximately 60–75% of cases. Studies have shown a reduced rate of cesarean delivery in patients who have undergone external cephalic version compared with controls. Although complications of external cephalic version are uncommon, they include placental abruption, cord prolapse, fetal distress, feto–maternal hemorrhage, stillbirth, and vaginal bleeding. Serious complications are rare. One large meta-analysis of 12,955 attempted cephalic versions reported serious complications in 0.24% of the participants and a need for emergency cesarean delivery in 0.35% of the participants.

The likelihood of success of external cephalic version is related to several factors (Box 128-1). Women with characteristics associated with success are ideal candidates. There are, however, some absolute contraindications to external cephalic version. In conditions where vaginal delivery is contraindicated, such as prior classical cesarean delivery, placenta previa, and Category III fetal heart rate pattern, external cephalic version should not be performed.

External cephalic version should not be performed before 36 completed weeks of gestation. Given the possibility (although remote) of the need for emergency cesarean delivery, the risks of prematurity are lower after 36 weeks of gestation compared with before 36 weeks of gestation. A randomized trial of external cephalic version at 34–35 weeks of gestation versus 37 or more weeks of gestation found that although there were more cephalic presentations at birth when done at the earlier gestational age, the rate of cesarean delivery was not reduced. A meta-analysis suggested that early external cephalic version is associated with an increased risk of preterm delivery.

Women with a prior low transverse cesarean delivery may be offered an external cephalic version. Limited data have shown comparable success rates without adverse outcomes. Anterior placenta location, although not as favorable as posterior location, is not a contraindication for

BOX 128-1

Factors Associated With Successful External Cephalic Version

- Increasing parity
- Increasing amniotic fluid volume
- Posterior placenta
- Unengaged presenting part
- Fetal head easily palpable
- Relaxed uterus

external cephalic version. If intrauterine growth restriction is present, it may not be prudent to recommend the procedure. An amniotic fluid index of 10 cm at 35 weeks of gestation is lower than average, but is within the normal range and is not a contraindication.

American College of Obstetricians and Gynecologists. External cephalic version. ACOG Practice Bulletin 13. Washington, DC: ACOG; 2000.

Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Breech presentation and delivery. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams obstetrics. 23rd ed. New York (NY): McGraw-Hill Medical Publishing Division; 2010. p. 527–43.

Grootscholten K, Kok M, Oei SG, Mol BW, van der Post JA. External cephalic version–related risks: a meta-analysis. Obstet Gynecol 2008; 112:1143–51.

Hutton EK, Hannah ME, Ross SJ, Delisle MF, Carson GD, Windrim R, et al. The Early External Cephalic Version (ECV) 2 Trial: an international multicentre randomised controlled trial of timing of ECV for breech pregnancies. Early ECV2 Trial Collaborative Group. BJOG 2011;118:564–77.

Kok M, Bais JM, van Lith JM, Papatsonis DM, Kleiverda G, Hanny D, et al. Nifedipine as a uterine relaxant for external cephalic version: a randomized controlled trial. Obstet Gynecol 2008;112:271–6.

129

Chorioamnionitis

A 38-year-old woman, gravida 1, comes to the labor and delivery unit at term with ruptured membranes and early labor. Six hours later, her contractions are regular, she is 7 cm dilated, and she requests intravenous narcotics for her discomfort. Her heart rate is 110 beats per minute and her temperature is 38.2°C (100.8°F). Her uterine fundus is noted to be tender between contractions. The fetal heart rate is 160 beats per minute at baseline but has moderate variability and no decelerations. The best next step in management is

(A) immediate cesarean delivery
(B) administration of acetaminophen and cool compresses
* (C) administration of intravenous antibiotics
(D) culture the amniotic fluid using an intrauterine pressure catheter

Chorioamnionitis or intra-amniotic infection is diagnosed clinically. The classic definition is a fever of 38°C (100.4°F) and at least two other findings: maternal or fetal tachycardia or both, maternal leukocytosis, uterine tenderness, and foul-smelling amniotic fluid. Chorioamnionitis is associated with premature rupture of membranes, prolonged labor, multiple examinations, and the absence of other causes of these signs and symptoms. The incidence of clinical chorioamnionitis is estimated to be in the 1–4% range at term, with a higher incidence in preterm deliveries. Given that chorioamnionitis is microbial, culture or Gram stain is not used.

Placental pathology does not consistently correlate with the clinical diagnosis of intra-amniotic infection. Histology confirms the diagnosis of clinical chorioamnionitis in only 62% of cases. See Table 129-1 for clinical criteria for the diagnosis of chorioamnionitis. Histologic funisitis is believed to be related to fetal infection and correlates more strongly with risk of neonatal sepsis. Fever without other evidence of infection has been found in higher rates in women who receive epidural anesthesia.

The vast majority of intra-amniotic infections are due to ascending bacteria into the uterus from the lower genital tract. However, some organisms that cause intra-amniotic infection, such as listeria, can be bloodborne, and others (eg, ureaplasma) can cross intact membranes.

The diagnosis of clinical chorioamnionitis is associated with a variety of morbidities for the mother and neonate. Higher rates of dysfunctional labor, cesarean delivery, and postpartum hemorrhage are associated with intra-amniotic infection. It is postulated that beyond association, these outcomes may occur because of direct effects of infection on myometrial contractility. Mothers experience higher rates of postpartum endomyometritis and wound infection. For the neonate, in utero infection can result in both short-term and long-term complications. Neonatal sepsis, pneumonia, depression at birth, intraventricular hemorrhage, and death are more immediate complications. Cerebral palsy and developmental delay are seen in higher rates in infants with chorioamnionitis.

Use of immediate intrapartum broad spectrum antibiotics decreases the risk of maternal and neonatal infec-

TABLE 129-1. Clinical Diagnosis of Chorioamnionitis

Test Clinical Parameters	Result Suggesting Chorioamnionitis	Comments Generally Nonspecific
Fever	Temperature greater than 38°C (100.4°F) twice or greater than 38.3°C (101°F) once	95–100% sensitive
Maternal tachycardia	Greater than 100 bpm	50–80% sensitive
Fetal tachycardia	Greater than 160 bpm	40–70% sensitive
Fundal tenderness	Tenderness on palpation	4–25% sensitive
Vaginal discharge	Foul-smelling discharge	5–22% sensitive

Abbreviation: bpm, beats per minute.

Tita AT, Andrews WW. Diagnosis and management of clinical chorioamnionitis. Clin Perinatol 2010;37:339–54. Copyright 2010 by Elsevier.

tious complications compared with postpartum–neonatal therapy. Traditionally ampicillin and gentamicin have been used because of placental passage and coverage of typical causative agents for neonatal sepsis. Alternatives, such as ampicillin–sulbactam are acceptable. Some health care providers advocate the addition of anaerobic coverage at cesarean delivery for maternal benefit. Postpartum treatment should be individualized based on clinical circumstances.

Duration of time after intrapartum diagnosis and treatment of chorioamnionitis until delivery is not correlated to neonatal outcome. Cesarean delivery should be reserved for obstetric indications. Adjunctive supportive measures, such as acetaminophen and cool compresses to decrease maternal fever, may assist in resolving fetal tachycardia but have not been proved to directly benefit maternal and neonatal outcomes.

Gibbs RS. Management of clinical chorioamnionitis at term. Am J Obstet Gynecol 2004;191:1–2.

Hopkins L, Smaill FM. Antibiotic regimens for management of intraamniotic infection. Cochrane Database of Systematic Reviews 2002, Issue 3. Art. No.: CD003254. DOI: 10.1002/14651858.CD003254.

Premature rupture of membranes. ACOG Practice Bulletin No. 80. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;109:1007–19.

Tita AT, Andrews WW. Diagnosis and management of clinical chorioamnionitis. Clin Perinatol 2010;37:339–54.

Yoon BH, Romero R, Park JS, Kim M, Oh SY, Kim CJ, et al. The relationship among inflammatory lesions of the umbilical cord (funisitis), umbilical cord plasma interleukin 6 concentration, amniotic fluid infection, and neonatal sepsis. Am J Obstet Gynecol 2000;183:1124–9.

130

Cerebral palsy

A 33-year-old woman develops premature rupture of the fetal membranes at 25 weeks of gestation. She has no clinical signs of infection and is not in labor. She is treated with antenatal corticosteroids for fetal maturation and antibiotics to increase the duration of the latency period. The pharmacologic therapy that has been associated in this clinical scenario with a lower rate of cerebral palsy in surviving preterm neonates is

(A) terbutaline
(B) nifedipine
(C) indomethacin
* (D) magnesium sulfate
(E) nitroglycerin

Within the past 10 years, several large randomized clinical trials have been performed that have evaluated the effects of prenatal magnesium sulfate on cerebral palsy and neurodevelopmental outcomes in preterm neonates. Although the patient populations and magnesium sulfate regimens were slightly different, a meta-analysis of the results shows that the rate of cerebral palsy was lower in patients who received magnesium sulfate compared with patients who received placebo (see Appendix F).

In the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network study, most participants had preterm premature rupture of membranes (greater than 80%). This multicenter placebo-controlled randomized trial included 2,241 women at imminent risk of delivery between 24 weeks and 31 weeks of gestation. Magnesium sulfate was administered as a 6-g loading dose followed by a constant infusion of 2 g per hour for up to 12 hours. The study showed a 45% reduction in the rate of moderate to severe cerebral palsy in surviving infants (1.9% versus 3.5%; relative risk = 0.55; 95% confidence interval 0.32–0.95). Approximately 63 eligible women would need to be treated with magnesium sulfate in order to prevent one case of moderate to severe cerebral palsy in the neonate. Mild maternal adverse effects of magnesium sulfate were common but no major or life-threatening events occurred.

The American College of Obstetricians and Gynecologists and the Society for Maternal Fetal–Medicine have stated that physicians who elect to use magnesium sulfate for fetal neuroprotection should develop specific guidelines regarding inclusion criteria, treatment regimen, and the role of concordant tocolysis. One such algorithm has been published (Fig. 128-1). None of the other medications listed (ie, terbutaline, indomethacin, nifedipine, and nitroglycerin) have been shown to have any fetal neuroprotective properties.

Crowther CA, Hiller JE, Doyle LW, Haslam RR. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. Australasian Collaborative Trial of Magnesium Sulphate (ACTOMg SO4) Collaborative Group. JAMA 2003;290:2669–76.

Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD004661. DOI: 10.1002/14651858.CD004661.pub3; 10.1002/14651858.CD004661.pub3.

Magnesium sulfate before anticipated preterm birth for neuroprotection. Committee Opinion No. 455. American College of Obstetricians and Gynecologists; Society for Maternal–Fetal Medicine; Obstet Gynecol 2010;115:669–71.

Marret S, Marpeau L, Zupan–Simunek V, Eurin D, Leveque C, Hellot MF, et al. Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial*. PREMAG trial group. BJOG 2007;114:310–8.

Reeves SA, Gibbs RS, Clark SL. Magnesium for fetal neuroprotection. Am J Obstet Gynecol 2011;204:202.e1–4.

Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. Eunice Kennedy Shriver NICHD Maternal–Fetal Medicine Units Network. N Engl J Med 2008;359:895–905.

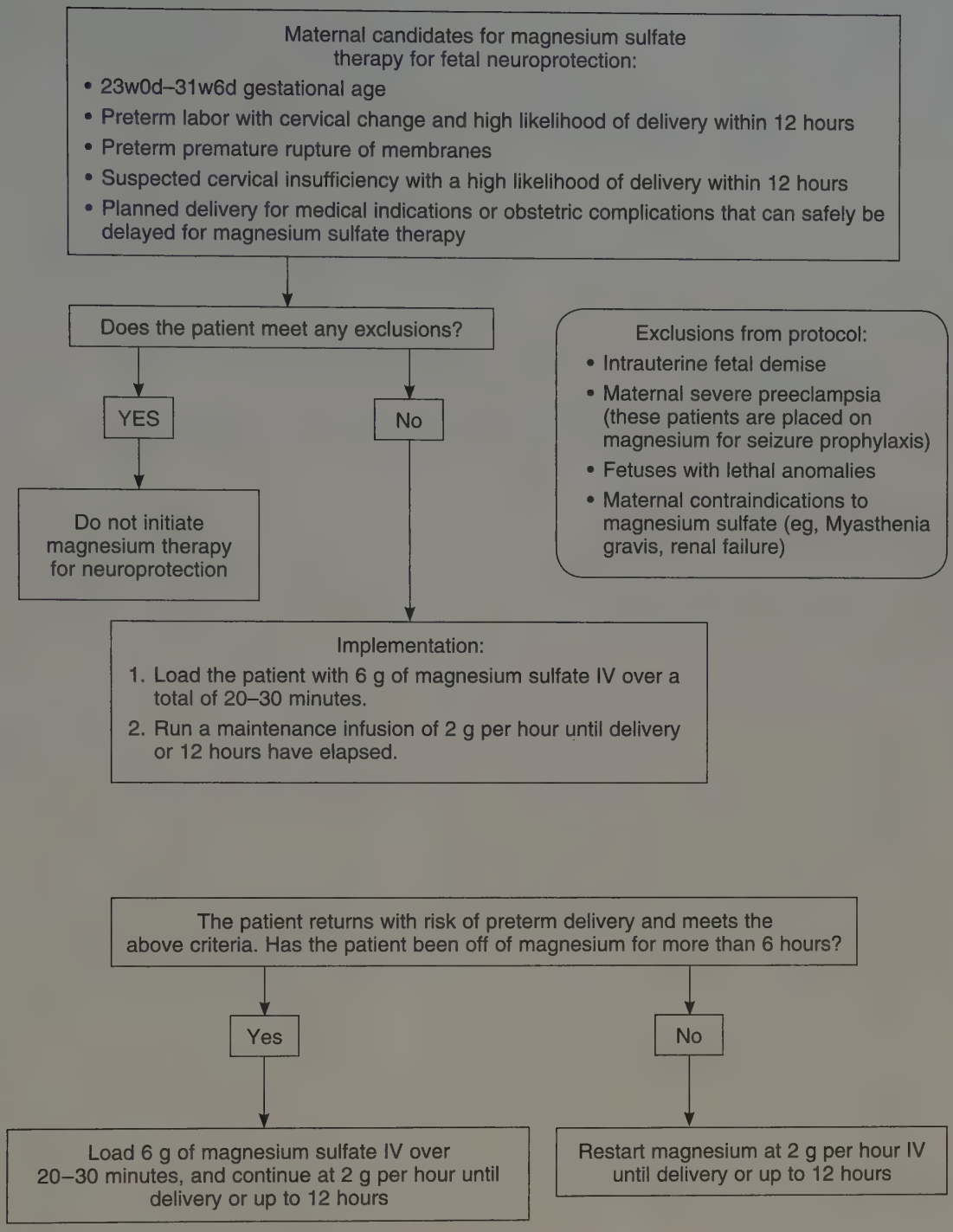

Maternal candidates for magnesium sulfate therapy for fetal neuroprotection:
• 23w0d–31w6d gestational age
• Preterm labor with cervical change and high likelihood of delivery within 12 hours
• Preterm premature rupture of membranes
• Suspected cervical insufficiency with a high likelihood of delivery within 12 hours
• Planned delivery for medical indications or obstetric complications that can safely be delayed for magnesium sulfate therapy
Does the patient meet any exclusions?
YES
No
Do not initiate magnesium therapy for neuroprotection
Exclusions from protocol:
• Intrauterine fetal demise
• Maternal severe preeclampsia (these patients are placed on magnesium for seizure prophylaxis)
• Fetuses with lethal anomalies
• Maternal contraindications to magnesium sulfate (eg, Myasthenia gravis, renal failure)
Implementation:
1. Load the patient with 6 g of magnesium sulfate IV over a total of 20–30 minutes.
2. Run a maintenance infusion of 2 g per hour until delivery or 12 hours have elapsed.
The patient returns with risk of preterm delivery and meets the above criteria. Has the patient been off of magnesium for more than 6 hours?
Yes
No
Load 6 g of magnesium sulfate IV over 20–30 minutes, and continue at 2 g per hour until delivery or up to 12 hours
Restart magnesium at 2 g per hour IV until delivery or up to 12 hours

FIG. 130-1. Algorithm for selection of candidates and administration of magnesium sulfate for fetal neuroprotection. (Reeves SA, Gibbs RS, Clark SL. Magnesium for fetal neuroprotection. Am J Obstet Gynecol 2011;204:202.e1–4.)

131–134

Hepatitis B

For each clinical interpretation (131–134), select the most likely laboratory values (A–E). (Abbreviations: anti-HBc, total hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; IgM anti-HBc: immunoglobulin M antibody to hepatitis B core antigen.)

(A) HBsAg negative, anti-HBc negative, anti-HBs positive
(B) HBsAg negative, anti-HBc positive, anti-HBs positive
(C) HBsAg negative, anti-HBc negative, anti-HBs negative
(D) HBsAg positive, anti-HBc positive, IgM anti-HBc positive, anti-HBs negative
(E) HBsAg positive, anti-HBc positive, IgM anti-HBc negative, anti-HBs negative

131. D. Acute infection with hepatitis B

132. B. Immune to hepatitis B due to natural infection

133. E. Chronic hepatitis B infection

134. A. Immune due to hepatitis B vaccination

Perinatal transmission of hepatitis B is one of the largest contributors to chronic hepatitis infection worldwide. When perinatal transmission occurs, 85–95% of those infected will have a risk of persistent or chronic infection, leading to a 25–30% risk of serious or fatal liver disease. Women who are seropositive for HBsAg alone have a 10–20% risk of neonatal transmission without neonatal prophylaxis. If, in addition, the hepatitis e antigen is positive, transmission approaches 90% in the absence of prophylaxis.

Preventive strategies, including active and passive neonatal immunization, can reduce the risk of infection in the newborn by approximately 85–95%. For this reason, routine screening of all pregnant women for hepatitis B infection is recommended. The obstetrician–gynecologist must therefore be familiar with the interpretation of the results of testing for hepatitis B. Routine screening in clinical practice for active or chronic hepatitis B infection is done with a test for HBsAg.

Serologic testing for hepatitis B infection can be confusing and may be more easily understood when visualized in graphic form. Figure 131–134-1 represents the serologic progression of acute hepatitis B infection. Hepatitis B surface antigen appears before clinical symptoms of hepatitis, and on average is detectable for 1–6 weeks. Antibodies to hepatitis B surface antigen increase during recovery for up to 10–12 months after HBsAg has cleared. In most patients with self-limited acute hepatitis B infection, anti-HBs and HBsAg are not both present in the serum at the same time. There may be a window period in acute infection where HBsAg has been cleared but anti-HBs is not yet detectable. In this case, hepatitis B infection can be diagnosed by the presence of anti-HBc with IgM anti-HBc, and this indicates an infection within the past 6 months (option D). Antibodies to core antigen are only present in natural infection. In clinical practice it is not routine to test for anti-HBc.

With immunity to hepatitis B from natural infection (option B), anti-HBs and anti-HBc remain positive. This is in contrast to immunity from vaccination (option A) where only anti-HBs is present.

In chronic hepatitis B infection, a different serologic pattern is present (option E). Figure 131–134-2 depicts the serologic response. Persistence of HBsAg is present, but antibodies to the surface antigen (anti-HBs) are not detectable. Additionally, antibodies to core antigen (anti-HBc) are present but IgM antibodies are negative, which indicates that this is not an acute or recent infection. In individuals who are chronically infected with hepatitis B, the presence of HBeAg denotes greater infectivity.

In the case of a serologic profile that is negative for HBsAg, anti-HBs, and anti-HBc (option C), the individual has neither had natural infection nor detectable antibodies from vaccination and, therefore, is susceptible to hepatitis B infection. Depending on age and risk factors, vaccination may be warranted.

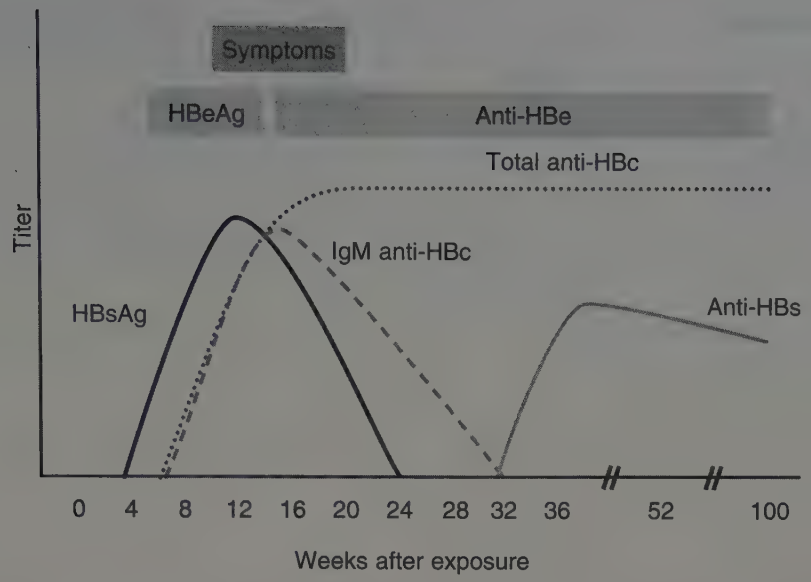


FIG. 131–134-1. Typical serologic course of acute hepatitis B virus infection with recovery. (Mast EE, Weinbaum CM, Fiore AE, Alter MJ, Bell BP, Finelli L, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC) [published erratum appears in MMWR Morb Mortal Wkly Rep 2007;56:1114]. MMWR Recomm Rep 2006;55:1–33; quiz CE1–4.)

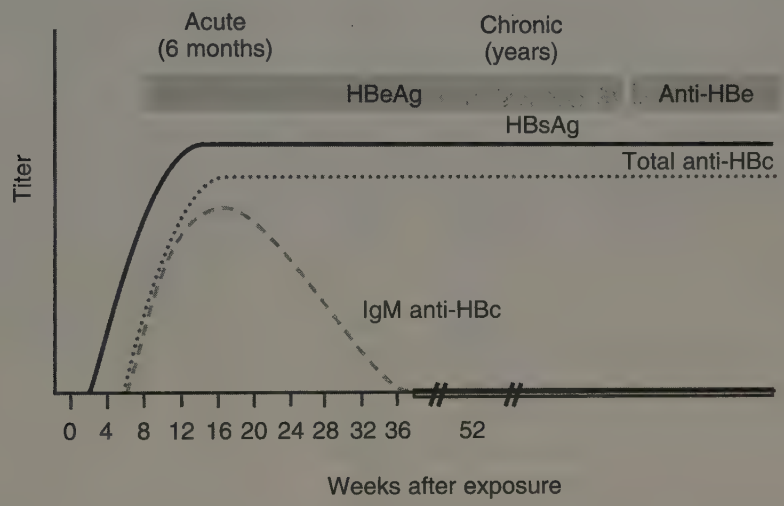


FIG. 131–134-2. Progression to chronic hepatitis B virus infection: typical serologic course. (Mast EE, Weinbaum CM, Fiore AE, Alter MJ, Bell BP, Finelli L, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC) [published erratum appears in MMWR Morb Mortal Wkly Rep 2007;56:1114]. MMWR Recomm Rep 2006;55:1,33; quiz CE1–4.)

Hepatitis B and hepatitis C virus infections in obstetrician–gynecologists. ACOG Committee Opinion No. 332. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006;107:1207–8.

Panda B, Panda A, Riley LE. Selected viral infections in pregnancy. Obstet Gynecol Clin North Am 2010;37:321–31.

Viral hepatitis in pregnancy. ACOG Practice Bulletin No. 86. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;110:941–56.

135–138

Aneuploidy screening

For each test characteristic (135–138), select the corresponding first-trimester and second-trimester integrated aneuploidy screening protocol (A–D).

(A) Independent sequential
(B) Stepwise sequential
(C) Contingent sequential
(D) Complete integrated

135. A. Highest false-positive rate

136. C. Most cost-effective in an entire population

137. D. Patients not informed of results in the first trimester

138. A. Highest detection rate

All pregnant women should be offered screening or diagnostic testing for aneuploidy before 20 weeks of gestation. Second-trimester serum screening, such as the quadruple screen to measure alpha-fetoprotein, unconjugated estriol, human chorionic gonadotropin, and inhibin A, is typically offered at 15–20 weeks of gestation. This test provides a detection rate of approximately 80% with a 5% false-positive rate.

The addition of first-trimester screening to the available options has allowed for earlier and more accurate detection of fetal chromosomal abnormalities. It also presents more choices for testing paradigms. First-trimester combined screening describes the use of serum screening (β-hCG and pregnancy-associated plasma protein-A) with ultrasonographically determined nuchal translucency. The combined test provides a detection rate of 82–87%, with a 5% false-positive rate. Other than improved sensitivity, the other advantage of combined screening over second-trimester screening is that the results are available earlier. With earlier results, it is possible to choose chorionic villous sampling, which will provide definitive results in the first trimester.

Several paradigms exist for screening that combine first-trimester and second-trimester testing, ie, integrated screening (Table 135–138-1). Serum integrated testing combines serum analysis of pregnancy-associated plasma protein-A in the first trimester with results from quadruple analyte testing in the second trimester, providing an improved detection rate (85–88%) over the quadruple screen alone. Complete integrated screening, which adds the first-trimester nuchal translucency measurement, achieves a 94–96% detection rate with a false-positive rate of 5%. The weakness with this paradigm is that patients are not informed of results in the first trimester, negating the benefits of first-trimester screening.

Sequential screening potentially overcomes this by informing the patients at highest risk in the first-trimester screening process, giving them an opportunity for early invasive diagnostic testing (eg, by chorionic villous sampling). Patients at low risk continue to the second-trimester serum testing, which is combined to give an overall risk assessment with improved sensitivity than if independent first-trimester or second-trimester screening alone was used. Three different options are possible:

1. Independent sequential screening involves ordering a first-trimester screening test, followed by a separate quadruple test in the second trimester. The two tests are not integrated and the second-trimester results are not calculated with reference to the first-trimester results. Although this method results in a high detection rate (98%), the false-positive rate is as high as 17%.
2. In stepwise sequential screening, diagnostic testing is offered to patients with high-risk results (eg, greater than 1:50) in the first trimester, whereas all other patients go on to second-trimester screening. This paradigm has detection rates similar to complete integrated screening.
3. Contingent sequential screening offers diagnostic testing in the first trimester for high-risk patients. Low-risk patients (eg, less than 1:2,000) have no need for further testing. Patients with intermediate risk (1:50 to 1:2,000) will need to receive later integrated testing. This paradigm may be the most cost-effective, with detection rates of 88–94% and a false-positive rate of 5%, depending on the particular cutoffs used.

TABLE 135–138-1. Testing Paradigms for Aneuploidy Screening

	Detection Rate	False-Positive Rate	Results in First Trimester	Components
Quadruple screen	80–83%	5%	No	Second trimester: AFP, uE3, hCG, inh-A
Serum integrated	85–88%	5%	No	First trimester: PAPP-A Second trimester: AFP, uE3, hCG, inh-A
Complete integrated	94–96%	5%	No	First trimester: NT, PAPP-A Second trimester: AFP, uE3, hCG, inh-A
Independent sequential	98%	17%	Yes	First trimester: NT, PAPP-A, hCG Second trimester: AFP, uE3, hCG, inh-A
Contingent sequential	88–94%	5%	Yes, to patients with high-risk results	First trimester: NT, PAPP-A Second trimester: AFP, uE3, hCG, inh-A (second trimester tests done only in patients with intermediate risk results)
Stepwise sequential	95%	5%	Yes, to patients with high-risk results	First trimester: NT, PAPP-A, hCG Second trimester: AFP, uE3, hCG, inh-A

Abbreviations: AFP, alpha-fetoprotein; hCG, human chorionic gonadotropin; inh-A, inhibin A; NT, nuchal translucency; PAPP-A, pregnancy-associated plasma protein-A uE3, unconjugated estriol.

Canick JA. New choices in prenatal screening for Down syndrome. OBG Manage 2005;17(12):38–44, 47.

Malone FD, Canick JA, Ball RH, Nyberg DA, Comstock CH, Bukowski R, et al. First-trimester or second-trimester screening, or both, for Down's syndrome. First- and Second-Trimester Evaluation of Risk (FASTER) Research Consortium. N Engl J Med 2005;353:2001–11.

Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin No. 77. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;109:217–27.

Wald NJ, Rodeck C, Hackshaw AK, Walters J, Chitty L, Mackinson AM. First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS). SURUSS Research Group. Health Technol Assess 2003;7:1–77.

139–143

Immunization in pregnancy

A 26-year-old woman comes to your office for her first prenatal visit at 10 weeks of gestation, and you review her vaccination history with her. She reports that she does not have any risk factors for infections for which she could be vaccinated. The area in which she lives has not reported any increase of particular pathogens. For each vaccine (139–143), identify the appropriate timing for its administration (A–D) in this pregnant woman.

(A) Postpartum
(B) Any time during pregnancy
(C) First trimester only
(D) After 20 weeks of gestation

139. B. Influenza vaccine

140. D. Diphtheria and reduced tetanus toxoids and acellular pertussis vaccine (Tdap)

141. A. Varicella vaccine

142. A. Measles, mumps, rubella vaccine

143. B. Hepatitis A vaccine

Vaccinations are a critical part of routine health care, and several new recommendations have been made related to vaccinations in pregnancy. In general, these recommendations are less restrictive than prior guidelines and encourage consideration of the potential for harm from vaccination versus exposure. One notable exception to this is the human papillomavirus vaccine. The Centers for Disease Control and Prevention specifically notes that no adverse outcomes have been associated with use of the human papillomavirus vaccine in pregnancy, although because of the paucity of data the Centers for Disease Control and Prevention still recommends that the series be withheld or interrupted until after the pregnancy is completed.

Inactivated influenza vaccine should be administered during pregnancy in any trimester during the influenza season. The live activated influenza vaccine (nasal spray) should not be administered during pregnancy. Pregnant women are at significant increased risk of serious consequences of influenza compared with nonpregnant women. The increased morbidity related to influenza during pregnancy is related to physiologic changes that include decreased pulmonary volume, increased cardiac output, and suppression of cell-mediated immunity. A randomized controlled trial demonstrated immunization benefits to both mother and child, such as 30% less respiratory febrile illnesses in mothers and 63% fewer cases of influenza in newborns. An increase in adverse consequence of inactivated influenza vaccine in pregnant women or their offspring compared with nonpregnant controls has not been reported.

In 2005, Tdap (which contains tetanus toxoid, reduced inactivated diphtheria toxoid, and acellular pertussis) was licensed in 2005 for individuals aged 11–64 years in the United States and extended to permissive receipt for individuals aged 65 years and older. As with other vaccines, Tdap immunization should be recommended in the preconception period. Pregnancy is not a contraindication to Tdap immunization but it should be administered after 20 weeks of gestation. When Tdap is administered during pregnancy, transplacental maternal antibodies provide some protection to the infant.

Live attenuated varicella vaccine has been demonstrated to be safe in preventing chickenpox in adults. Varicella vaccine is contraindicated in pregnant women because it is live attenuated. If a woman accidentally receives the varicella vaccine within a month of conception or in pregnancy, the incidence of fetal infection and complications does not appear to be increased from baseline, and termination should not be recommended.

Similar to varicella vaccine, the measles, mumps, rubella vaccine also is live attenuated, and should not be administered to pregnant women, but should be administered to rubella-seronegative women in the postpartum period. Seronegative women (for either varicella, rubella, or both) who are postpartum, and who present for a preconception visit or for infertility treatment, should be offered appropriate vaccination.

Hepatitis A vaccine is an inactive two-dose vaccine. It can be safely used during pregnancy if a patient is at risk of hepatitis A exposure. Hepatitis A vaccine also is available in a three-dose combination with hepatitis B vaccine. Immunity after vaccination lasts greater than 10 years.

Centers for Disease Control and Prevention. Guidelines for vaccinating pregnant women: abstracted from recommendations of the Advisory Committee on Immunization Practices (ACIP). Atlanta (GA): CDC; 2012. Available at: http://www.cdc.gov/vaccines/pubs/downloads/b_preg_guide.pdf. Retrieved June 11, 2012.

Influenza vaccination during pregnancy. Committee Opinion No. 468. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:1006–7.

Recommended adult immunization schedule—United States, 2011. Centers for Disease Control and Prevention. MMWR Morb Mortal Wkly Rep 2011;60:1–4.

Update on immunization and pregnancy: tetanus, diphtheria, and pertussis vaccination. ACOG Committee Opinion No. 521. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;119:690–1.

Zaman K, Roy E, Arifeen SE, Rahman M, Raqib R, Wilson E, et al. Effectiveness of maternal influenza immunization in mothers and infants [published erratum appears in N Engl J Med 2009;360:648]. N Engl J Med 2008;359:1555–64.

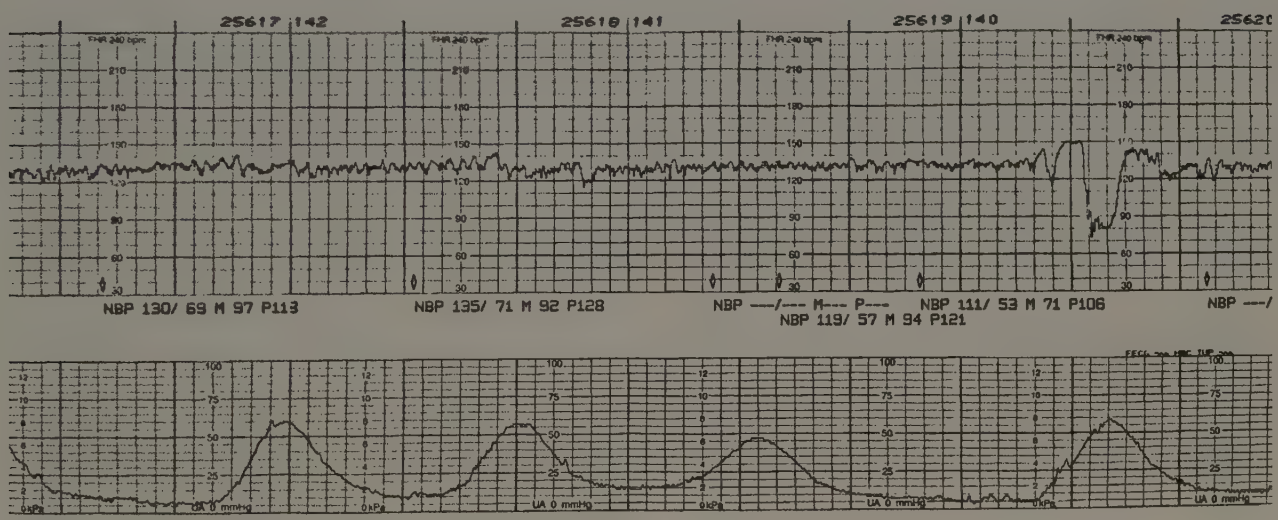
144–148

Intrapartum electronic fetal monitoring nomenclature

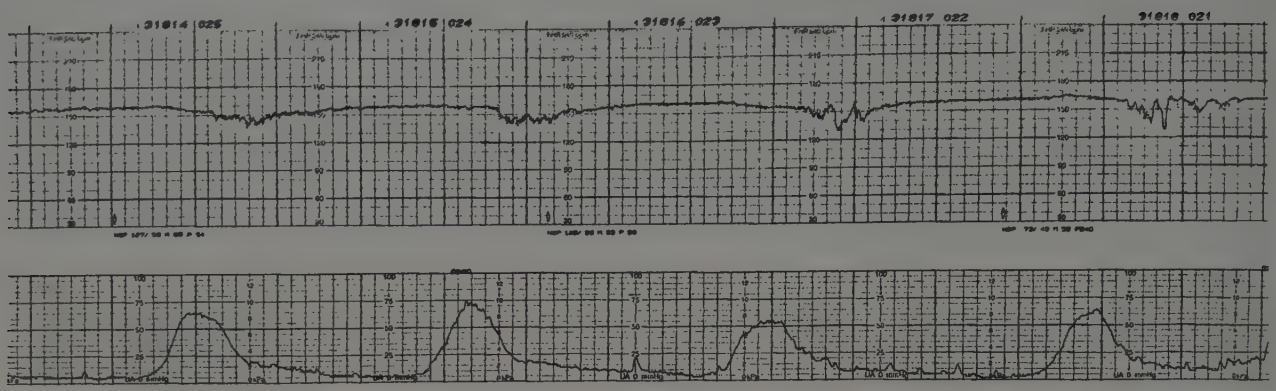
For each clinical scenario (144–148), choose the most likely fetal heart rate tracing pattern (A–D).

(A) Category I
(B) Category II
(C) Category III
(D) Uninterpretable

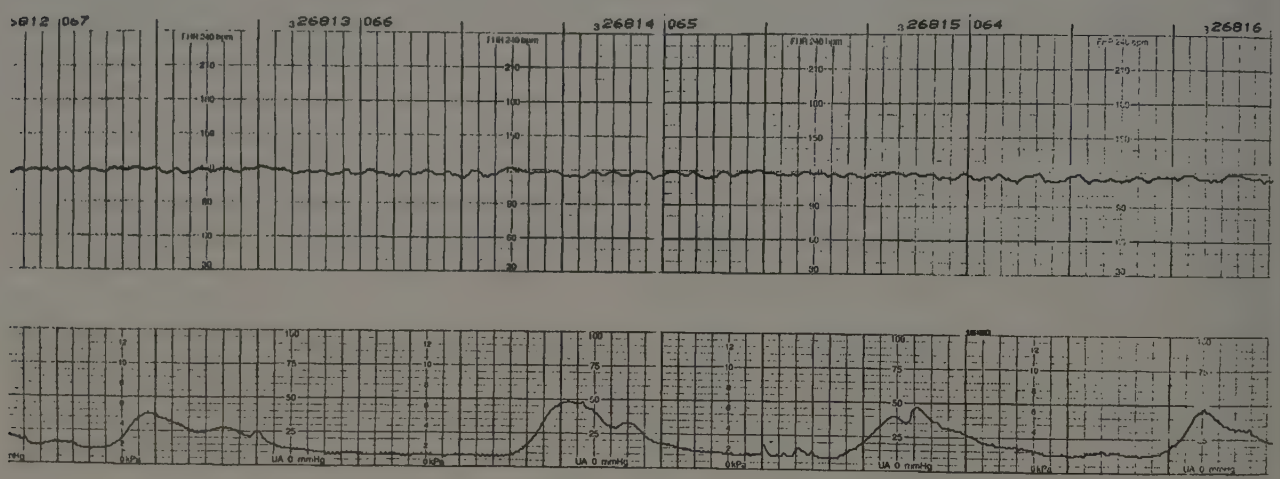
144. B. A 23-year-old woman at 38 weeks of gestation who receives oxytocin for augmentation of labor after admission for premature rupture of membranes.



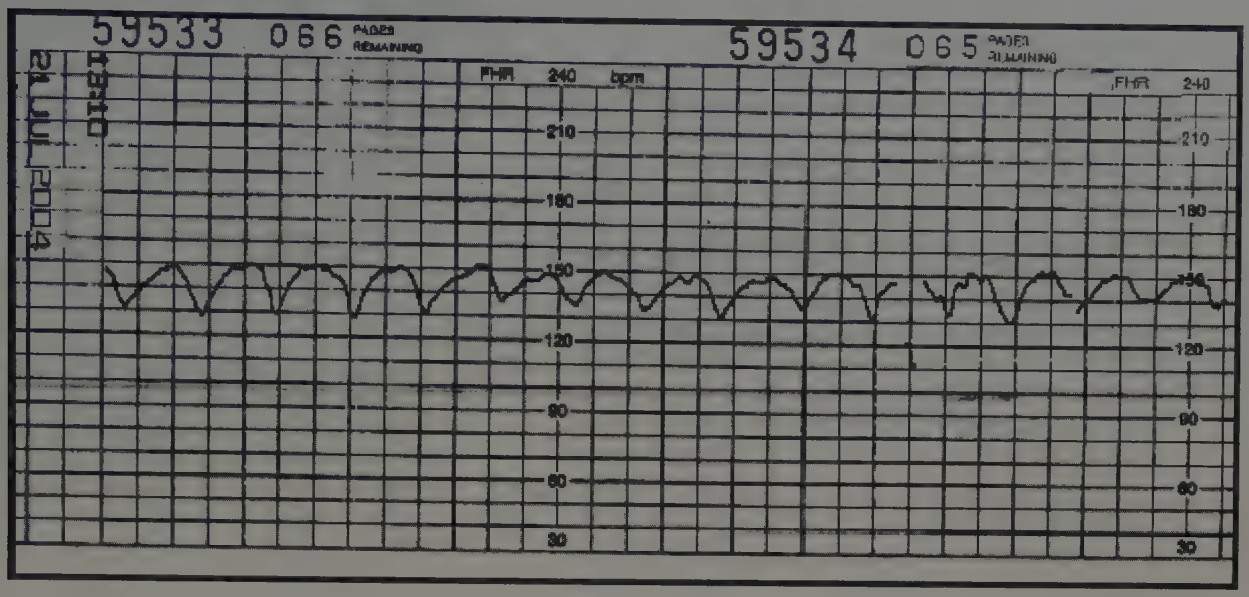
145. A 32-year-old woman, gravida 3, para 2, at 37 weeks of gestation is in labor; she has a history of chronic hypertension and pregnancy complicated by fetal growth restriction.



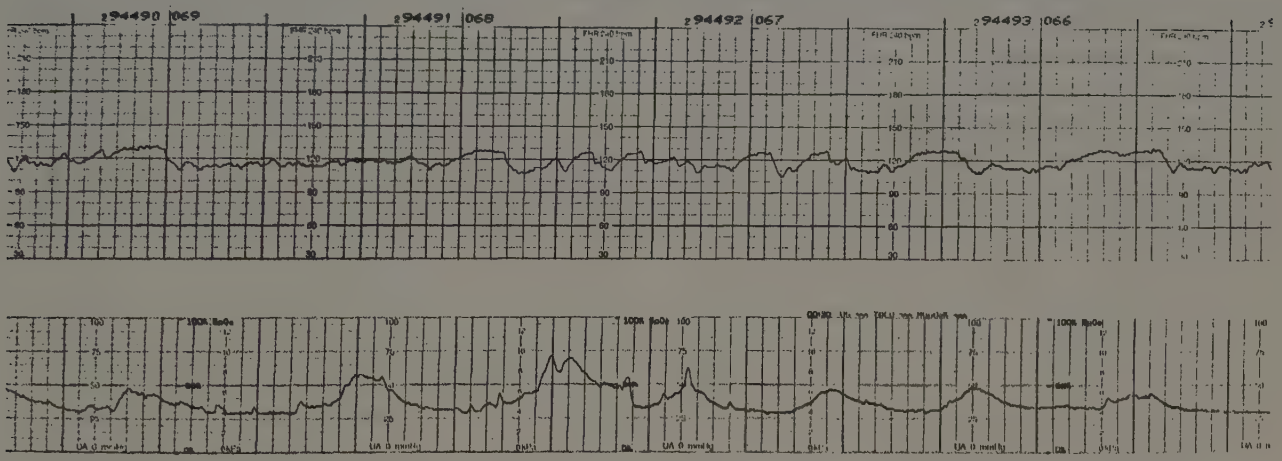
146. An 18-year-old woman, 5 cm dilated, 30 minutes after she received epidural anesthesia.



147. A 23-year-old woman at 38 weeks of gestation, who presents with contractions, rupture of membranes, and vaginal bleeding. Vaginal examination demonstrates a cervix that is 4 cm dilated and 100% effaced, with fetal vertex at 0 station.



148. A 28-year-old woman, gravida 3, para 0, at 40 weeks of gestation admitted in active labor.



Electronic fetal heart rate (FHR) monitoring has been integrated into common practice in the United States as an assessment tool for fetal well-being. Continuous intrapartum electronic monitoring is recommended for high-risk pregnancies, whereas intermittent monitoring is suggested for uncomplicated pregnancies. Evidence suggests that intrapartum FHR monitoring reduces neonatal seizures, but it has no effect on cerebral palsy or fetal mortality rates. Its use may result in higher cesarean delivery and operative vaginal delivery rates. Although FHR monitoring effectively identifies normoxic and normally adapted fetuses, it is less specific at identifying abnormal fetal physiologic conditions. For instance, out of 1,000 abnormal FHR tracings only one to two tracings will identify a neonate who will develop cerebral palsy.

The 1997 National Institutes of Health National Institute of Child Health and Human Development workshop for electronic fetal monitoring established uniform nomenclature and definitions to guide health care providers to use a standard system of pattern interpretation. The recommendations standardized terms for baseline rates (normal, tachycardia, bradycadia), variability, accelerations, decelerations, and contraction patterns. The primary value was to provide a common language for communication and documentation.

In 2008, further recommendations were added to the

original guidelines. For the most part, definitions of decelerations and baselines remained unchanged. One important change was the quantification of uterine contractions, now considered as the number of contractions present in a 10-minute window, averaged over 30 minutes. More than five contractions in a 10-minute period is defined as tachysystole; the terms hyperstimulation and hypertonus are no longer used.

A three-tiered interpretation system was introduced in 2008 to aid in reading, communicating, and managing intrapartum FHR tracings (Box 144–148-1). Accelerations are not necessary to classify a Category I tracing. Furthermore, early decelerations are acceptable for Category I. Although most FHR assessments will likely be classified in Category II, the presence of moderate variability or accelerations are reassuring features, whereas the absence of both requires close surveillance and expedited management. Appendix E-1–E-2 describes management guidelines for different FHR tracing categories.

The FHR tracing in Scenario 144 demonstrates a normal baseline, moderate variability, and a variable deceleration (Category II). In Scenario 145, there is absent variability and recurrent late decelerations (Category III). The FHR patterns in Scenarios 146 and 148 show normal baselines, moderate variability, no decelerations, and absence of accelerations (Category I). The sinusoidal FHR tracing of Scenario 147 may indicate fetal anemia (Category III).

Electronic fetal heart rate monitoring: research guidelines for interpretation. National Institute of Child Health and Human Development Research Planning Workshop. Am J Obstet Gynecol 1997;177: 1385–90.

Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. ACOG Practice Bulletin No. 106. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:192–202.

Macones GA, Hankins GD, Spong CY, Hauth J, Moore T. The 2008 National Institute of Child Health and Human Development workshop report on electronic fetal monitoring: update on definitions, interpretation, and research guidelines. Obstet Gynecol 2008;112:661–6.

Management of intrapartum fetal heart rate tracings. Practice Bulletin No. 116. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010;116:1232–40.

Neilson JP. Fetal electrocardiogram (ECG) for fetal monitoring during labour. Cochrane Database of Systematic Reviews 2012, Issue 4. Art. No.: CD000116. DOI: 10.1002/14651858.CD000116.pub3.

BOX 144-148-1

Three-Tiered Interpretation System to Aid in Reading, Communicating, and Managing Fetal Heart Rate Tracings

A. Category I (normal). Strongly predictive of normal fetal acid–base status, these FHR tracings may be followed in a routine manner and include all of the following:
- Baseline rate 110–160 beats per minute
- Moderate variability
- Absent late or variable decelerations
- Early decelerations may or may not be present
- Accelerations may or may not be present

B. Category II (indeterminate). Not predictive of abnormal fetal acid–base status but requiring evaluation, continued surveillance, and re-evaluation, taking into account the clinical context. This category includes any of the following:
- Baseline rate
  - — Bradycardia not accompanied by absent baseline variability
  - — Tachycardia
- Baseline FHR variability
  - — Minimal baseline variability
  - — Absent baseline variability not accompanied by recurrent decelerations
  - — Marked baseline variability
- Accelerations
  - — Absence of induced accelerations after fetal stimulation
- Periodic or episodic decelerations
  - — Recurrent variable decelerations accompanied by minimal or moderate baseline variability
  - — Prolonged deceleration of 2 minutes or more but less than 10 minutes
  - — Recurrent late decelerations with moderate baseline variability
  - — Variable decelerations with other characteristics, such as slow return to baseline, "overshoots," or "shoulders"

C. Category III (abnormal). Predictive of abnormal fetal acid–base status; requires prompt evaluation and management. Includes either of the following:
- Absent baseline FHR variability with:
  - — Recurrent late decelerations
  - — Recurrent variable decelerations, or
  - — Bradycardia
- Sinusoidal FHR

Modified from Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. ACOG Practice Bulletin No. 106. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;114:192–202.

149–151

Maternal and fetal adverse effects of tocolysis

For each clinical scenario (149–151), choose the drug (A–D) that is most likely associated with it.

(A) Terbutaline
(B) Nifedipine
(C) Magnesium sulfate
(D) Indomethacin

149. A. A 39-year-old woman at 31 weeks of gestation develops cardiac arrhythmias during prolonged treatment for recurrent preterm labor.

150. D. A 27-year-old woman at 26 weeks of gestation develops oligohydramnios after 5 days of tocolytic therapy.

151. C. A 16-year-old girl at 25 weeks of gestation develops flushing, headache, and lethargy 6 hours after the initiation of tocolytic therapy.

Preterm birth is the leading cause of neonatal mortality. Approximately 12% of births in the United States are preterm. The incidence of preterm birth has slightly decreased over the past few years but still remains one of the most significant complications of pregnancy. Treatment of preterm labor is controversial. Tocolytic drugs may prolong pregnancy for approximately 2–7 days. This short-term prolongation of pregnancy may be beneficial to the neonate in providing time for the administration of corticosteroids for fetal lung maturation and maternal transport to a facility with an appropriate level of neonatal intensive care. Tocolytic treatment beyond 2 days after corticosteroids have been administered is of unclear benefit.

There is no drug of choice for tocolysis and all drugs have limited benefit and potential adverse effects. Studies report conflicting evidence of effectiveness between beta-mimetics, magnesium sulfate, calcium channel blockers, and nonsteroidal antiinflammatory agents. Choice of drug should be individualized based on maternal comorbidities and the potential adverse effects of the drug. If tocolytic agents are used, the obstetrician–gynecologist should be familiar with the adverse effects of the different agents. Pulmonary edema has been associated with the use of β-mimetics, magnesium sulfate, and calcium channel blockers. Appendix G lists various tocolytic agents by mechanism of action and adverse effects.

Terbutaline is a β-mimetic drug used in pregnancy as a treatment for preterm labor as well as in acute cases of uterine hyperstimulation to relax the uterus. Terbutaline has known cardiovascular effects and its use is contraindicated in women with a history of cardiac arrhythmias. Reported neonatal effects include hyperinsulinemia, myocardial hypertrophy, septal hypertrophy, and myocardial ischemia. Recently, the U.S. Food and Drug Administration (FDA) issued a "black box" warning for the use of terbutaline in pregnancy. The FDA has advised health care professionals to be aware that after prolonged administration of oral or injectable terbutaline, there have been reports of death and serious adverse reactions including increased heart rate, transient hyperglycemia, hypokalemia, cardiac arrhythmias, pulmonary edema, and myocardial ischemia. Parenteral terbutaline should not be used outside the hospital setting. Oral terbutaline is not recommended for maintenance tocolysis. The FDA acknowledges that there may be obstetric conditions in which a physician may decide that the benefit of terbutaline for an individual hospitalized patient may outweigh the risk.

Nifedipine is a calcium channel blocker commonly used for the treatment of preterm labor. It has been found to have fewer adverse effects than β-mimetic agents such as terbutaline. Studies have shown that in well-hydrated, normotensive pregnant women, nifedipine does not significantly affect blood pressure. Calcium channel blockers cause peripheral vasodilation and induce an increase in sympathetic tone leading to cardiac stimulation by increasing heart rate. Blood pressure and uterine blood flow is maintained through an increase in cardiac output. Calcium channel blockers should be used with caution in patients with cardiac disease, renal diseases and maternal hypotension (blood pressure less than 90/50 mm Hg). Flushing, headache, nausea, pulmonary edema, and transient hypotension have been reported as adverse effects.

In the practice of obstetrics, magnesium sulfate is used not only as a tocolytic agent but also for seizure

prophylaxis in women with preeclampsia. Use for neonatal neuroprotection is another potential indication. Magnesium sulfate is contraindicated in women with myasthenia gravis. It should be used with caution with renal impairment. The adverse effects of flushing and headache overlap with those of calcium channel blockers. However, high levels of magnesium sulfate are also associated with lethargy, muscle weakness, diplopia, dry mouth, pulmonary edema, and cardiopulmonary arrest. Fetal adverse effects include lethargy, hypotonia, and respiratory depression.

Prostaglandin synthetase inhibitors, such as indomethacin, also are used as tocolytics. They are reported to have the fewest maternal adverse effects. However, fetal adverse effects of such medications include oligohydramnios and premature narrowing of the ductus arteriosus. Neonatal intraventricular hemorrhage, hyperbilirubinemia, and necrotizing enterocolitis also have been associated with indomethacin use. Use should be limited to short courses of 48 hours or less before 32 weeks of gestation. The oligohydramnios that occurs as a consequence of indomethacin use generally is reversible.

Conde-Agudelo A, Romero R, Kusanovic JP. Nifedipine in the management of preterm labor: a systematic review and metaanalysis. Am J Obstet Gynecol 2011;204:134.e1–20.

Cornette J, Duvekot JJ, Roos-Heselink JW, Hop WCJ, Steegers EAP. Maternal and fetal haemodynamic effects of nifedipine in normotensive pregnant women. BJOG: An International Journal of Obstetrics & Gynaecology 2011;118:510–5.

Food and Drug Administration. FDA drug safety communication: new warnings against use of terbutaline to treat preterm labor [press release]. Rockville (MD): FDA; 2011. Available at: http://www.fda.gov/drugs/drugsafety/ucm243539.htm. Retrieved May 31, 2012.

Management of preterm labor. Practice Bulletin No. 127. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;119:1308.

152–154

Fetal acid–base assessment

Select the umbilical artery blood gas interpretation (A–D) that goes best with the clinical scenario (152–154).

(A) Mixed acidemia (umbilical artery pH, 6.94; P_{CO_2}, 94 mm Hg; P_{O_2}, 12 mm Hg, base excess, –18 mEq/L).
(B) Metabolic acidemia (umbilical artery pH, 7.05; P_{CO_2}, 40 mm Hg; P_{O_2}, 30 mm Hg; base excess, –16 mEq/L).
(C) Normal (umbilical artery pH, 7.29; P_{CO_2}, 46 mm Hg; P_{O_2}, 40 mm Hg; base excess, –1 mEq/L).
(D) Respiratory acidemia (umbilical artery pH, 7.09; P_{CO_2}, 65 mm Hg; P_{O_2}, 20 mm Hg, base excess, –6 mEq/L).

152. D. A 35-year-old woman with a term pregnancy and Category I fetal heart rate (FHR) tracing undergoes amniotomy in labor and develops an umbilical cord prolapse followed by fetal bradycardia of 90 beats per minute. Emergent cesarean delivery occurs 14 minutes later. The baby is delivered with Apgar 7 at 1 minute and Apgar 8 at 5 minutes.

153. C. A 30-year-old woman with a term pregnancy progresses to complete dilation with station at +3. She is exhausted from pushing for 3 hours. The FHR is 150 beats per minute with moderate variability and an occasional variable deceleration that lasts 45 seconds and descends 45 beats below the baseline. Operative vaginal delivery is performed and the newborn is vigorous at birth.

154. A. A 24-year-old woman at 37 weeks of gestation comes to the hospital with vaginal bleeding, severe abdominal pain, a hypertonic uterus, and fetal bradycardia. She had a prior cesarean delivery. She is stabilized and is taken for emergent repeat cesarean delivery. The fetus is delivered 22 minutes later. The newborn develops seizures shortly after birth and meets the criteria for therapeutic hypothermia.

Umbilical cord blood gas measurement is the most objective method to assess fetal acid–base status immediately before birth. It is a better predictor of neonatal outcomes than either FHR patterns or Apgar scores. Normative ranges have been described for both the umbilical artery and vein for term pregnancies (Table 152–154-1). Compared with values from the umbilical vein, umbilical arterial pH, P_{O_2}, and base excess are lower, and P_{CO_2} is higher. Assessment of both umbilical arterial and venous blood gas analysis is recommended in the following clinical situations:

- Cesarean delivery for fetal compromise
- Low 5-minute Apgar score (less than 7)
- Severe fetal growth restriction
- Abnormal FHR tracing
- Maternal thyroid disease
- Intrapartum fever
- Multifetal gestation

Respiratory acidemia is diagnosed when the umbilical pH is decreased along with increased P_{CO_2} and a normal base excess. This pattern can be found with short-term or relatively mild episodes of decreased fetal blood flow as in a prolapsed cord (Case 152). Low umbilical pH, ie, pH less than 7.0, is a poor predictor of adverse outcome in the setting of a normal base excess. Cord prolapse is an acute event; the most likely blood gas interpretation (if delivery is expeditious) would be respiratory acidosis.

The most sensitive indicator of fetal acid–base status is FHR variability. The presence of moderate variability, even in the presence of recurrent decelerations (eg, early, variable, or late) is associated with normal fetal arterial pH (Case 153).

Mixed acidemia most often is caused by prolonged uncompensated respiratory acidemia (Case 154). It is associated with decreased pH, increased P_{CO_2}, and decreased base excess. An umbilical arterial pH value at birth less than 7.0 combined with a base excess greater than –12 mmol/L is part of the essential criteria to

TABLE 152–154-1. Umbilical Cord Blood pH and Blood Gas Values in Normal Term and Preterm Newborns in Various Studies

Values	Ramin et al., 1989*† (n = 1,292)	Riley and Johnson, 1993*† (n = 3,522)	Ariken et al., 2000* (n = 1,281)¶
Arterial Blood			
pH	7.28 (0.07)	7.27 (0.069)	7.25 (7.08)‡
Pco_2 (mm Hg)	49.9 (14.2)	50.3 (11.1)	50.0 (75)¶
Hco_3 (mEq/L)	23.1 (2.8)	22.0 (3.6)	–
Base excess (mEq/L)	–3.6 (2.8)	–2.7 (2.8)	–4.3 (–11.1)¶
Venous Blood			
pH	–	7.34 (0.063)	–
Pco_2 (mm Hg)	–	40.7 (7.9)	–
Hco_3 (mEq/L)	–	21.4 (2.5)	–
Base excess (mEq/L)	–	–2.4 (2.0)	–

Abbreviations: pH, hydrogen ion concentration; Pco_2, partial pressure of carbon dioxide; Hco_3, bicarbonate concentration.

*Ramin SM, Gilstrap LC 3rd, Leveno KJ, Burris J, Little BB. Umbilical artery acid-base status in the preterm infant. Obstet Gynecol 1989;74:256–8; Riley RJ, Johnson JW. Collecting and analyzing cord blood gases. Clin Obstet Gynecol 1993;36:13–23; and Arikan GM, Scholz HS, Petru E, Haeusler MC, Haas J, Weiss PA. Cord blood oxygen saturation in vigorous infants at birth: what is normal? BJOG 2000;107:987–94.

†Infants of selected women with uncomplicated vaginal deliveries.

‡Infants of unselected women with vaginal deliveries.

Shown as mean (SD).

¶Shown as median and 2.5 or 97.5 percentile.

Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Williams obstetrics. 23rd edition. New York (NY): McGraw-Hill Medical Publishing Division; 2010. p. 596. This material is reproduced with permission of the McGraw-Hill Companies. Copyright McGraw-Hill 2010.

establish whether hypoxemia proximate to delivery was severe enough to be associated with acute neurologic injury.

Andres RL, Saade G, Gilstrap LC, Wilkins I, Witlin A, Zlatnik F, et al. Association between umbilical blood gas parameters and neonatal morbidity and death in neonates with pathologic fetal acidemia. Am J Obstet Gynecol 1999;181:867–71.

Hankins GD, Speer M. Defining the pathogenesis and pathophysiology of neonatal encephalopathy and cerebral palsy. Obstet Gynecol 2003;102:628–36.

Low JA. Intrapartum fetal asphyxia: definition, diagnosis, and classification. Am J Obstet Gynecol 1997;176:957–9.

Thorp JA, Sampson JE, Parisi VM, Creasy RK. Routine umbilical cord blood gas determinations? Am J Obstet Gynecol 1989;161:600–5.

Umbilical cord blood gas and acid-base analysis. ACOG Committee Opinion No. 348. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006;108:1319–22.

155–159

Hemoglobinopathy

Match the hemoglobin electrophoresis results (A–E) with the most likely diagnosis of anemia (155–159).

(A) Hemoglobin A, 91%; A_2, 5%; and F, 4%.
(B) Hemoglobin A, 58%; A_2, 2%; S, 39%; and F, 1%.
(C) Hemoglobin A, 97%; A_2, 2%; and F, 1%.
(D) Hemoglobin A, 10%; A_2, 1%; S, 85%; and F, 4%.
(E) Hemoglobin A, 30%; A_2, 5%; S, 62%; and F, 3%.

155. C. α-thalassemia

156. A. β-thalassemia

157. D. Sickle cell disease

158. E. Sickle β-thalassemia

159. B. Sickle cell trait

The normal hemoglobin structure consists of a tetramer of four interlocking polypeptide chains. Each chain attaches to the heme molecule. The four types of polypeptide chains in fetal and adult hemoglobin are alpha, beta, delta, and gamma. Characteristics of hemoglobin A, hemoglobin A_2, and hemoglobin F are outlined in Box 155–159-1.

Inherited hemoglobin disorders constitute the most common monogenic disease. Approximately 7% of the world population are hemoglobinopathy carriers of the disease and approximately 300,000–400,000 affected babies are born each year. The highest frequency of hemoglobinopathies is in the tropical regions. However, because of population migration, hemoglobinopathies are today encountered in almost every country. Individuals of African descent are at risk for all types of hemoglobinopathies. Alpha-thalassemia is more common in individuals of Southeast Asian, Mediterranean, and West Indian descent, and β-thalassemia is more common in individuals of Asian, Mediterranean, Middle Eastern, Hispanic, and West Indian descent.

Sickle cell disease is a group of autosomal recessive disorders that results from hemoglobin S. Hemoglobin A is changed to hemoglobin S by the substitution of valine for glutamic acid in the β-chain. Classically, individuals with sickle cell disease are homozygous for hemoglobin S, in which case, the disorder is called sickle cell anemia. Sickle cell trait is distinguished from sickle cell anemia by the amount of hemoglobin S present. Hemoglobin S is typically less than 50% in carriers and 85–95% in individuals with sickle cell anemia. Hemoglobin S combined with another abnormal hemoglobin, such as hemoglobin C or β-thalassemia, can result in a similar clinical phenotype as sickle cell anemia. The best diagnostic test for patients with sickle cell disease is hemoglobin electrophoresis. Solubility tests, such as sickle prep or Sickledex, detect hemoglobin S but fail to differentiate between the heterozygous and homozygous state and fail to detect other abnormal hemoglobin chains, such as hemoglobin C. Table 155–159-1 shows the typical electrophoresis patterns in individuals with sickle cell trait, sickle cell anemia, and sickle-β-thalassemia.

Beta-thalassemia is caused by a reduction (β^+) or the absence (β^0) of β-globulin chain. Three clinical conditions are recognized: mild, moderate, and severe anemia (Table 155–159-2). The β-thalassemia carrier state is clinically asymptomatic. Red blood cells are microcytic and hypochromic and the hemoglobin electrophoresis has specific characteristics: hemoglobin A_2 greater than 3.5 g/dL, and increased hemoglobin F. Beta-thalassemia minor or carrier state is the most common form encountered during pregnancy; β-thalassemia major or Cooley anemia is the most severe form of β-thalassemia. The complete lack of normal β-globulin chain production causes a life-threatening anemia that requires regular

BOX 155-159-1

Classifications of Hemoglobin

A	Two α-chains and two β-chains
A_2	Two α-chains and two δ–chains
F	Two α-chains and two γ-chains

TABLE 155–159-1. Electrophoretic Patterns in Common Hemoglobinopathies

	Hemoglobin A	Hemoglobin S	Hemoglobin C	Hemoglobin F	Hemoglobin A_2
Normal	95–98*	0	0	<1	2.5 ± 0.2
Sickle cell trait	50–60	35–45†	0	<2	Less than 3.5
β-thalassemia	90–95	0	1–3	1–3	Greater than 3.5
Sickle-β^+-thalassemia	5–30	65–90	0	2–10	Greater than 3.5
Sickle-β^0-thalassemia	0	80–92	0	2–15	Greater than 3.5
β-hemoglobin C disease	0	45–50	45–50	1–8	Less than 3.5
Sickle cell anemia	0	85–95	0	2–15	Less than 3.5

Abbreviations: β^0, absence of β-hemoglobin chain; β^+, reduction of β-hemoglobin chain.

*Numbers indicate the percent of total hemoglobin for an untransfused adult patient. Ranges are approximate and may vary depending on the particular laboratory and method of determination.

†Percent of hemoglobin S can be as low as 21% in patients with sickle cell trait in conjunction with α-thalassemia.

Schrier SL, Landaw SA, Mentzer WC, Mahoney DH Jr. Introduction to hemoglobin mutations. http://www.uptodate.com/contents/introduction-to-hemoglobin-mutations. Copyright 2010 by UptoDate.

blood transfusions and extensive continuous medical care. Complications from ongoing blood transfusion, such as infection and iron-overload, ultimately lead to a premature death in the fourth decade. Beta-thalassemia intermedia is usually a less severe form of anemia than β-thalassemia major, but usually requires an occasional blood transfusion. However, β-thalassemia intermedia can be very heterogeneous and the clinical picture may range from severe anemia to being asymptomatic.

The four clinical forms of α-thalassemia are shown in Table 155–159-3. The carrier state is characterized by deletion in either one or both of the α-chains. Carriers of one abnormal α-chain are clinically unrecognizable and carriers of two abnormal α-chains typically have a mild microcytic, hypochromic anemia. Carriers of two abnormal genes may have a mutation on the same chromosome (*cis*) or on different chromosomes (*trans*). Individuals of Asian descent more commonly have the deletion on the same chromosome (*cis*), whereas individuals of African descent usually have the deletion on a different chromosome (*trans*). Individuals with hemoglobin H have an abnormality in three out of four α-chains that can clinically cause moderate to severe microcytic, hypochromic anemia. If all four α-chains are abnormal, the fetus has hemoglobin Bart disease. This form of α-thalassemia usually presents in utero as nonimmune hydrops fetalis and is lethal. Hemoglobin Bart is a rare disease but is more common in individuals of Asian descent because they typically carry the *cis* mutation. Individuals with α-thalassemia have a normal hemoglobin electrophoresis and require additional molecular testing to confirm the diagnosis.

TABLE 155–159-2. Characteristics of β-Thalassemia

	Genotype	Anemia
Silent carrier	β/β^+	Mild
Trait	β/β^0	Mild
Intermedia	β^+/β^+ or β^+/β^0	Moderate
Major	β^0/β^0	Severe

Abbreviations: β^0; absence of β-hemoglobin chain; β^+; reduction of β-hemoglobin chain.

TABLE 155–159-3. Characteristics of α-Thalassemia

	Genotype	Anemia
Silent carrier	αα/α–	None
Trait	αα/– (cis)	
	α–/α– (trans)	Mild
Hemoglobin H	α–/–	Moderate
Hemoglobin Bart	–/–	Fetal hydrops (lethal)

Cao A, Galanello R. Beta-thalassemia. Genet Med 2010;12:61–76.

Galanello R, Cao A. Gene test review. Alpha–thalassemia. Genet Med 2011;13:83–8.

Hemoglobinopathies in pregnancy. ACOG Practice Bulletin No. 78. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007;109:229–37.

Ram KT, Klugman SD. Best practices: antenatal screening for common genetic conditions other than aneuploidy. Curr Opin Obstet Gynecol 2010;22:139–45.

Thalassaemia International Federation. Guidelines for the clinical management of thalassaemia. 2nd revised ed. Nicosia, Cyprus: Thalassaemia International Federation; 2008. Available at: http://www.thalassaemia.org.cy/pdf/Guidelines_2nd_revised_edition_EN.pdf. Retrieved June 10, 2012.

Weatherall DJ, Clegg JB. Inherited haemoglobin disorders: an increasing global health problem. Bull World Health Organ 2001;79:704–12.

160–163

Use of peak flow meter in asthma

For each pregnant patient (160–163) with a preexisting diagnosis of asthma, choose the most appropriate plan of management (A–E).

(A) Continue current regimen
(B) Take two puffs of albuterol every 20 minutes for two treatments and re-evaluate peak expiratory flow rate (PEFR) in 1 hour
(C) Add inhaled corticosteroid
(D) Come to office for evaluation
(E) Use home nebulizer every 30 minutes and re-evaluate PEFR in 4 hours

160. C. A 17-year-old primigravid girl is at 20 weeks of gestation with a medication regimen of inhaled albuterol as necessary and before exercise. Her best PEFR is 400 L/min. At present, her PEFR is 300 L/min, and she has been using her inhaler four times a day for the past week. The school nurse asks you to evaluate her because she requests to be excused from gym class.

161. B. A 26-year-old multiparous woman at 30 weeks of gestation is managed on salmeterol–fluticasone. Her personal best PEFR is 320 L/min, but her PEFR has been 220 L/min over the past 2 days. She has no other medical problems at the time of her prenatal visit.

162. A. A 35-year-old multiparous woman at 32 weeks of gestation is managed on salmeterol–fluticasone. Her personal best PEFR is 280 L/min. Since her most recent prenatal visit, her PEFR has been 250 L/min. She reports no other medical problems at this time.

163. D. A 38-year-old primigravid woman at 33 weeks of gestation is treated with salmeterol–fluticasone. Her personal best PEFR is 300 L/min. She feels somewhat short of breath and her PEFR is presently 175 L/min despite her taking reserve albuterol. She telephones you to ask what she should do next.

Asthma is a common disease that frequently coexists with pregnancy, and management is not altered by the fact of pregnancy. Principles of asthma control include four crucial components defined by the National Heart, Lung and Blood Institute:

1. Measures of assessment and monitoring, obtained by objective tests, physical examination, patient history, and patient report to diagnose and assess the characteristics and severity of asthma and to monitor whether asthma control is achieved and maintained
2. Education for a partnership in asthma care
3. Control of environmental factors and comorbid conditions that affect asthma
4. Pharmacologic therapy

Objective measures of asthma severity and asthma control are easily obtained with the use of peak expiratory flow assessment, using a hand-held peak flow meter. This measurement correlates well with the forced expiratory volume in 1 second, which is the parameter measured in the pulmonary function laboratory. Objective measurements are important because a patient's perception of airflow is variable, physical examination is not always accurate, and treatment can be adjusted early in the course of deterioration. The patients most likely to benefit from peak flow monitoring are those with moderate or severe asthma, those with a history of severe exacerbations, and those with limited ability to perceive changes in their condition.

Asthma self-management and education should be reinforced at every opportunity. Self-management of asthma involves symptom recognition, self-monitoring, environmental control, drug treatment, and a written asthma action plan. Examples of written plans are downloadable from the National Heart, Lung and Blood Institute web site at http://www.nhlbi.nih.gov/health/public/lung/asthma/asthma_actplan.pdf. The action plan incorporates instructions for both daily asthma management and management of worsening asthma. Figure 160–163-1 shows an algorithm for managing exacerbations of asthma.

Environmental triggers should be assessed and, where the patient is known to be sensitive, exposure should be avoided. Such triggers may include outdoor

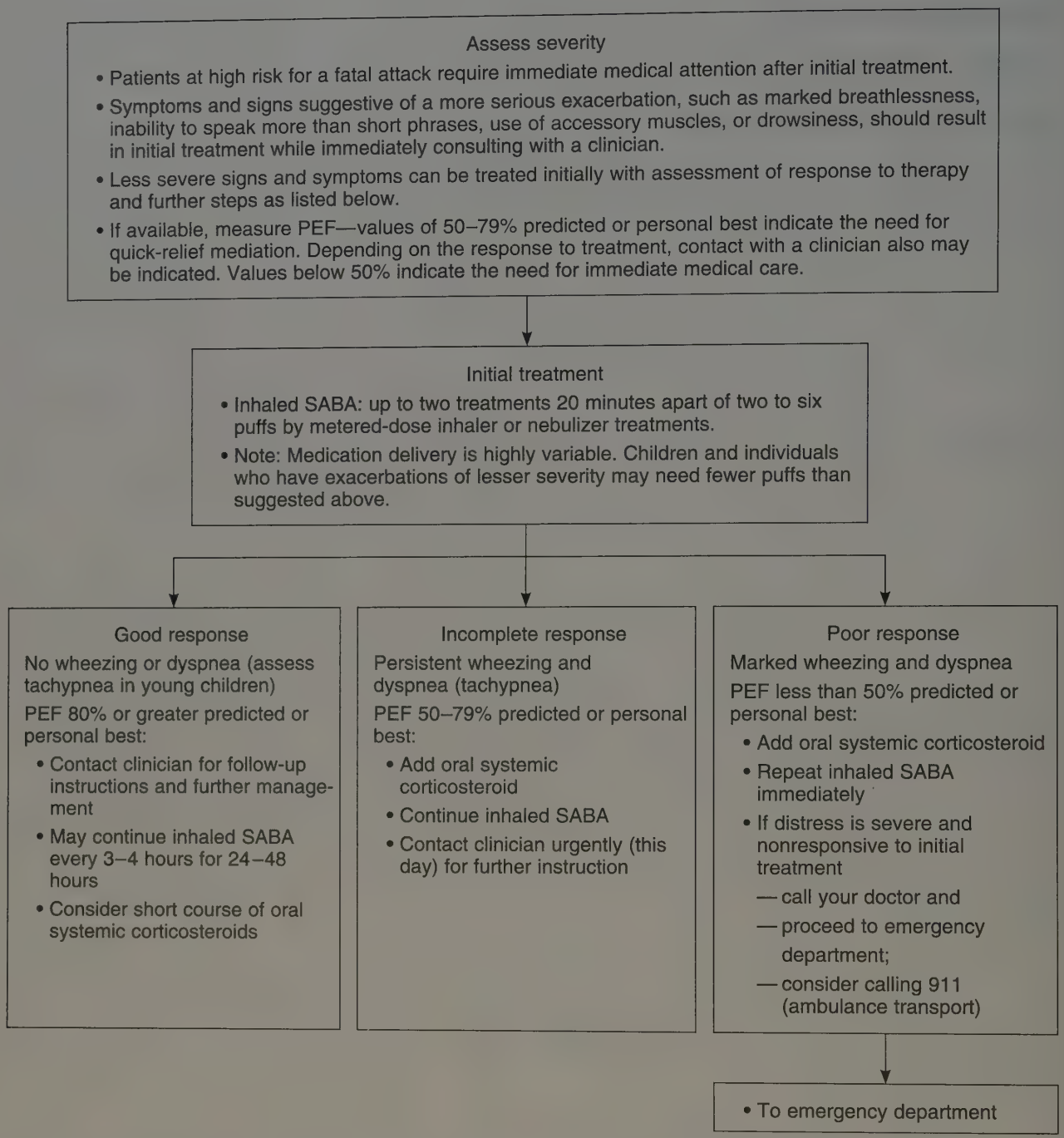

Assess severity
• Patients at high risk for a fatal attack require immediate medical attention after initial treatment.
• Symptoms and signs suggestive of a more serious exacerbation, such as marked breathlessness, inability to speak more than short phrases, use of accessory muscles, or drowsiness, should result in initial treatment while immediately consulting with a clinician.
• Less severe signs and symptoms can be treated initially with assessment of response to therapy and further steps as listed below.
• If available, measure PEF—values of 50–79% predicted or personal best indicate the need for quick-relief mediation. Depending on the response to treatment, contact with a clinician also may be indicated. Values below 50% indicate the need for immediate medical care.
Initial treatment
• Inhaled SABA: up to two treatments 20 minutes apart of two to six puffs by metered-dose inhaler or nebulizer treatments.
• Note: Medication delivery is highly variable. Children and individuals who have exacerbations of lesser severity may need fewer puffs than suggested above.
Good response
No wheezing or dyspnea (assess tachypnea in young children)
PEF 80% or greater predicted or personal best:
• Contact clinician for follow-up instructions and further management
• May continue inhaled SABA every 3–4 hours for 24–48 hours
• Consider short course of oral systemic corticosteroids
Incomplete response
Persistent wheezing and dyspnea (tachypnea)
PEF 50–79% predicted or personal best:
• Add oral systemic corticosteroid
• Continue inhaled SABA
• Contact clinician urgently (this day) for further instruction
Poor response
Marked wheezing and dyspnea
PEF less than 50% predicted or personal best:
• Add oral systemic corticosteroid
• Repeat inhaled SABA immediately
• If distress is severe and nonresponsive to initial treatment
— call your doctor and
— proceed to emergency department;
— consider calling 911 (ambulance transport)
• To emergency department

FIG. 160–163-1. Management of asthma exacerbations: home treatment. Abbreviations: PEF, peak expiratory flow; SABA, short-acting β_2-agonist (quick-relief inhaler). (National Institutes of Health: National Heart, Lung and Blood Institute. Expert panel report no. 3: guidelines for the diagnosis and management of asthma. Full report 2007. Bethesda, MD: U.S. Department of Health and Human Services. Available at http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed February 28, 2011.)

seasonal allergies, indoor pet allergens, and house mite or cockroach sensitization. Women with asthma should not smoke and should avoid exposure to secondhand smoke. Occupational exposures should be assessed. Air-conditioning and dehumidification of indoor air may be helpful. Outdoor activity should be avoided when air quality is poor.

Asthma medications may be stepped up as needed or stepped down when control is adequate. These recommendations are not affected by pregnancy. Although mild, intermittent, or exercise-induced asthma can be managed solely with inhaled β_2-agonists as needed, the mainstay of pharmacologic management for asthma is inhaled corticosteroids. No other agent is better for long-term asthma

control. Thus, for a patient who is not already using an inhaled corticosteroid, the next step in therapy is to add one. This decision may be driven either by an increase in the patient's symptoms or a decrease in her peak flow.

Patients should be taught to recognize worsening signs and symptoms of asthma and to begin quick-relief medication (short-acting β_2-agonist) when they do. A patient whose PEFR is below 80% of predicted or personal best needs intervention, and should begin by taking quick-relief medication. There is no difference in efficacy between a properly used metered-dose inhaler and home nebulizer treatment.

For exacerbations in which PEFR is 50–79% of predicted or personal best, the patient may self-administer a short-acting β_2-agonist, such as albuterol, either using a metered dose inhaler (two to six puffs) or using a nebulizer every 20 minutes for one to two treatments. If the response is good (PEFR 80% of personal best or greater), the patient may continue inhaled bronchodilators every 3–4 hours for up to 48 hours, and contact her physician. If the response is incomplete and PEFR remains 50–79%, the patient should start an oral steroid and call her doctor. If the patient's exacerbations are associated with a PEFR of less than 50% of her personal best, she should take an oral steroid and seek immediate medical care.

Patient 160, who normally has mild and exercise-induced asthma, now is more symptomatic than usual: she is using her quick-relief medication four times a day and recognizes she is short of breath with activity such as gym class. Even though her PEFR has not changed, she requires a step-up in therapy based on symptoms alone. This is an indication for an inhaled corticosteroid.

Although Patient 161 is asymptomatic, she has recently exhibited a decrease in PEFR to approximately 68% of her personal best: this is an exacerbation of airflow obstruction. Although it would be useful to determine what triggered the exacerbation, the appropriate response would be to treat it with quick-relief inhaled β_2-agonists.

Patient 162 has neither symptoms nor a significant decrement in her PEFR. Her PEFR of 250 L/min is 89% of her personal best (280 L/min). Although she has more severe disease than the other described patients, she is stable and needs no alteration in treatment.

Patient 163 is symptomatic, with a marked decrement in her PEFR (48% of personal best). She is likely to require evaluation in person. She may try quick-relief medications at home, but these medications are less successful with more severe exacerbations. The best course would be to begin oral steroids at home and come in immediately for assessment.

Cydulka RK. Acute asthma during pregnancy. Immunol Allergy Clin N Am 2006;26:103–17.

Dombrowski MP, Schatz M. ACOG practice bulletin: clinical management guidelines for obstetrician-gynecologists number 90, February 2008: asthma in pregnancy. ACOG Committee on Practice Bulletins–Obstetrics. Obstet Gynecol 2008;111(2 Pt 1):457–64.

National Asthma Education and Prevention Program Working Group Report. Managing asthma during pregnancy: recommendations for pharmacologic treatment. Update 2004. NIH Publication no. 05-5236, March 2005. U.S. Department of Health and Human Services. Bethesda, MD: National Institutes of Health: National Heart, Lung and Blood Institute. Available at http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg/astpreg_full.pdf. Accessed February 27, 2011.

National Institutes of Health: National Heart, Lung and Blood Institute. Expert panel report no. 3: guidelines for the diagnosis and management of asthma. Full report 2007. Bethesda, MD: U.S. Department of Health and Human Services. Available at http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed February 28, 2011.

Schatz M, Dombrowski MP. Asthma in pregnancy. N Engl J Med 2009;360:1862–9.

164–167

Contraindications to tocolysis

At a community hospital without neonatal intensive care unit capability, a 22-year-old woman, gravida 2, para 0, presents at 25 weeks of gestation with contractions. You find her cervix to be 3 cm dilated and 90% effaced. She is contracting every 5 minutes. You administer an initial dose of steroids and call for transport to a tertiary center. The accepting facility requests that she be given tocolysis before transport. In choosing the most appropriate tocolytic agent to use, you consider a number of factors, including contraindications. Match the contraindication (A–D) with the tocolytic agent (164–167).

(A) Oligohydramnios
(B) Hypotension
(C) Hypokalemia
(D) Myasthenia gravis

164. D. Magnesium sulfate

165. B. Nifedipine

166. C. Terbutaline

167. A. Indomethacin

Preterm birth remains one of the most vexing clinical problems in obstetrics. Although the rate of preterm birth has decreased slightly in recent years, preterm birth still represents approximately one in eight births in the most recent data available. Of pregnancies ending in a preterm birth, approximately 40–45% follow spontaneous preterm labor and another 25–30% follow preterm premature rupture of membranes; the remainder of these preterm deliveries are deliberately performed because of a medical or obstetric indication. Interventions to prevent preterm labor from progressing to preterm birth are limited. Many agents have been employed in order to attempt tocolysis, but a benefit in improving perinatal mortality has not been demonstrated. Agents include the β-adrenergic or β-mimetic drugs (terbutaline, ritodrine, fenoterol), magnesium sulfate, cyclooxygenase (COX) inhibitors (also referred to as prostaglandin synthetase inhibitors), calcium channel blockers, and oxytocin antagonists.

A systematic review of β-mimetics (versus placebo) used for tocolysis analyzed 11 randomized trials totaling 1,320 women. Although the number of women who gave birth within 48 hours was decreased by 37%, the benefit did not persist to 7 days, did not alter the risk of delivering preterm, and did not affect perinatal death, neonatal death, or the rate of serious complications in the newborn. Another systematic review of 23 randomized trials, which compared magnesium sulfate either to placebo or to an alternate tocolytic agent in a total of more than 2,000 women, found no difference in the rate of delivery within 48 hours, the rate of preterm delivery, or an improvement in perinatal outcome with magnesium sulfate.

Cyclooxygenase inhibitors also have been the subject of a systematic review. Indomethacin accounts for most trials, although sulindac, ketorolac, celecoxib have also been studied (as well as nimesulide and rofecoxib, which are unavailable in the United States). In most of these trials, COX inhibitors were compared with another tocolytic rather than with placebo. In a few small studies, the data suggest that COX inhibitors are more effective than placebo.

Calcium channel blockers, usually nifedipine, were found in a meta-analysis of 12 trials totaling greater than 1,000 women to be more efficacious than other tocolytics in prolonging pregnancy by 7 days and in prolonging pregnancy past 34 weeks of gestation. The risk reduction was modest. However, both COX inhibitors and calcium channel blockers are associated with lower rates of maternal adverse effects than β-mimetics. The oxytocin receptor antagonist atosiban, which is not available in the United States, has not been shown to be more successful than either placebo or β-mimetics in delaying birth, but it does have fewer adverse effects than β-mimetics.

Although tocolytic drugs do not prevent preterm birth, they may be effective in delaying delivery for several days. This may be useful in completing a course of steroids for fetal lung maturity or in transferring a patient

to a facility with better capabilities for care of a preterm newborn. In determining which agent to use, the physician must consider patient comorbidities, fluid status, and the adverse effect profile. Appendix G lists various tocolytic agents by mechanism of action and adverse effects.

Beta-mimetics are associated with maternal tachycardia, arrhythmia, hypotension, myocardial ischemia, pulmonary edema, hyperglycemia, and hypokalemia. Tremor, anxiety, and nausea also have been reported. The calcium channel blockers may cause hypotension, tachycardia, flushing, and headache. The COX inhibitors can constrict the renal arterioles, worsen asthma, and affect platelet function, in addition to the fetal effects of oligohydramnios and closure of the ductus arteriosus. Magnesium sulfate is contraindicated in myasthenia gravis because its effect on blocking acetylcholine release at the neuromuscular junction will worsen muscle weakness. The incidence of adverse events is higher with β-mimetics than with the other tocolytic drugs.

To conclude, magnesium sulfate is contraindicated in women with myasthenia gravis. It will potentiate preexisting muscle weakness and may be life threatening. Nifedipine is contraindicated if hypotension is already present because it lowers blood pressure. Terbutaline is contraindicated if hypokalemia is present because it lowers serum potassium. Indomethacin is contraindicated in the setting of oligohydramnios because it diminishes amniotic fluid production.

Anotayanonth S, Subhedar NV, Neilson JP, Harigopal S. Betamimetics for inhibiting preterm labour. Cochrane Database of Systematic Reviews 2004, Issue 4. Art. No.: CD004352. DOI: 10.1002/14651858.CD004352.pub2.

Crowther CA, Hiller JE, Doyle LW. Magnesium sulphate for preventing preterm birth in threatened preterm labour. Cochrane Database of Systematic Reviews 2002, Issue 4. Art. No.: CD001060. DOI: 10.1002/14651858.CD001060; 10.1002/14651858.CD001060.

de Heus R, Mol BW, Erwich JJ, van Geijn HP, Gyselaers WJ, Hanssens M, et al. Adverse drug reactions to tocolytic treatment for preterm labour: prospective cohort study. BMJ 2009;338:b744.

Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet 2008;371:75–84.

King JF, Flenady V, Cole S, Thornton S. Cyclo–oxygenase (COX) inhibitors for treating preterm labour. Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD001992. DOI: 10.1002/14651858.CD001992.pub2.

King JF, Flenady V, Papatsonis D, Dekker G, Carbonne B. Calcium channel blockers for inhibiting preterm labour. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No.: CD002255. DOI: 10.1002/14651858.CD002255.

Management of preterm labor. Practice Bulletin No. 127. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;119:1308.

Martin JA, Osterman MJ, Sutton PD. Are preterm births on the decline in the United States? Recent data from the National Vital Statistics System. NCHS Data Brief 2010;(39):1–8.

Papatsonis D, Flenady V, Cole S, Liley H. Oxytocin receptor antagonists for inhibiting preterm labour. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD004452. DOI: 10.1002/14651858.CD004452.pub2.

168–171

Acute fatty liver of pregnancy

Match the case presentation (168–171) with the most likely diagnosis (A–F).

(A) Acute fatty liver of pregnancy
(B) Acute viral hepatitis
(C) Cholestasis of pregnancy
(D) Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome
(E) Hemolytic uremic syndrome
(F) Thrombotic thrombocytopenic purpura

168. A. A 28-year-old primigravid woman with a twin gestation presents at 34 weeks of gestation with a 4-day history of anorexia, malaise, nausea, right upper quadrant pain, and headache. She is ill-appearing with a temperature of 37.4°C (99.4°F), blood pressure (BP) of 138/84 mm Hg, and icteric sclerae. Laboratory results show elevated white blood cell count and transaminase levels, 1+ proteinuria, platelet count of 164,000/mm^3, creatinine of 0.9 mg/dL, glucose of 52 mg/dL, fibrinogen of 108 mg/dL, and a prothrombin time of 32 seconds.

169. D. A 39-year-old woman, gravida 4, para 2, presents at 32 weeks of gestation with a 1-day history of epigastric pain, nausea, vomiting, and headache. She is afebrile and in moderate distress with a BP of 168/108 mm Hg. Laboratory results show 3+ proteinuria, lactate dehydrogenase of 720 international units/L, platelet count of 76,000/mm^3, creatinine of 1.0 mg/dL, aspartate aminotransferase of 132 international units/L, alanine aminotransferase of 141 international units/L, glucose of 84 mg/dL, and fibrinogen of 260 mg/dL.

170. F. A 31-year-old woman, gravida 2, para 1, presents at 27 weeks of gestation with headache, visual disturbance, abdominal pain, nausea, and vomiting. She has a temperature of 38.3°C (100.9°F) and BP of 146/91 mm Hg. Laboratory results include 2+ proteinuria, platelet count of 21,000/mm^3, lactate dehydrogenase of 1,552 international units/L, creatinine of 1.7 mg/dL, normal transaminase levels, and a normal coagulation panel.

171. B. A 23-year-old primigravid woman at 35 weeks of gestation presents with acute onset of malaise, anorexia, nausea, and right upper quadrant pain. She is afebrile with a BP of 124/68 mm Hg and her skin and sclerae are icteric. Laboratory results show negative urine protein, transaminase levels five times normal, total bilirubin of 3.4 mg/dL, creatinine of 0.6 mg/dL, platelet count of 194,000/mm^3, lactate dehydrogenase of 350 international units/L, and prothrombin time of 16 seconds.

The presence of elevated liver function tests in the third trimester is associated with several conditions that pose a variable risk to maternal and fetal well-being. The differential diagnosis includes entities that are unique to pregnancy, such as acute fatty liver of pregnancy, HELLP syndrome, and cholestasis of pregnancy. Disorders that are independent of pregnancy include acute viral hepatitis, hemolytic uremic syndrome (HUS), and thrombotic thrombocytopenic purpura (TTP). Clinical presentation and laboratory results are in most cases similar, but management and pregnancy outcomes may differ (Table 168–171-1).

Patient 168 presents with classic findings of acute fatty liver of pregnancy, which is a rare but potentially fatal condition seen in 1 in 10,000–15,000 deliveries. Risk factors include nulliparity and multiple gestation. Patients typically present during the third trimester with a 1-week to 2-week history of malaise, anorexia, nausea, vomiting, epigastric or right upper quadrant pain, headache, or jaundice. Physical findings may include an ill-appearing woman with low-grade fever, jaundice, and right upper quadrant or midepigastric tenderness. Neurologic findings may range from normal to lethargy, confusion, and even coma. Laboratory evaluation may reveal hemoconcentration, elevated white blood count, thrombocytopenia, hypofibrinogenemia, prolonged prothrombin time, hypoglycemia, hyperbilirubinemia and elevated creatinine, uric acid, liver enzyme, and ammonia levels.

TABLE 168–171-1. Differential Diagnosis of Acute Fatty Liver in Pregnancy

	Fatty Liver of Pregnancy	Acute Viral Hepatitis	HELLP Syndrome/ Preeclampsia/ Eclampsia	Cholestasis of Pregnancy	Hemolytic Uremic Syndrome	Thrombotic Thrombocytopenic Purpura
Onset (I/II/III trimester)	II/III, most greater than 35 weeks, rare reports less than 30 weeks	Any	II/III (after 20 weeks)	III, rare reports II	Any	Any, 60% less than 24 weeks
Clinical findings	Malaise, nausea/emesis, jaundice, mental status changes, abdominal pain, ± hemorrhage, ± preeclampsia	Malaise, nausea/ emesis, jaundice, abdominal pain	Malaise, hypertension, proteinuria, nausea, abdominal pain, rare jaundice ± seizures ± oliguria ± coagulopathy	Pruritus (worst in PM, palms and soles) ± jaundice	Hypertension, acute renal failure, nausea/ emesis, may have fever and neurologic findings, hallmarks microangiopathic anemia, severe thrombocytopenia	Often neurologic findings, fever and renal dysfunction, hallmarks microangiopathic anemia, severe thrombocytopenia
Laboratory						
Transaminases (units/mL)	↑Usually less than 500	↑Commonly greater than 1,000	Normal– ↑50× (more if liver hematoma)	↑(usually less than 300)	Usually normal ↑(unconjugated)	Usually normal ↑(unconjugated)
Bilirubin (mg/dL)	↑	±↑	↑occasionally (usually less than 2–3 times)	Often ↑(usually less than 5)	Usually normal	Usually normal
Prothrombin time Alkaline phosphatase	↑	±↑	Normal unless DIC/intrauterine fetal distress/abruptio placentae ↑occasionally	Usually normal, may be ↑ ↑(up to 4 times normal)	Usually normal	Usually normal
Other	↑Ammonia, very ↓ antithrombin III, ↓platelets, ↓fibrinogen, ↑WBC, ↑creatinine, proteinuria, ↓glucose	+ hepatitis serology, ↓antithrombin III	Moderately↓ antithrombin III, proteinuria,↓ platelets, ↑creatinine, ↑uric acid	↑serum bile acids	Normal antithrombin III, usually normal fibrinogen, ↑ WBC, ↓platelets (often less than 20,000), normal – slightly ↑ creatinine, ± proteinuria	Normal antithrombin III, usually normal fibrinogen, ↑ WBC, ↓platelets (often less than 20,000), normal – slightly ↑ creatinine, ± proteinuria
Liver histopathology	Centrilobular microvesicular fat, cholestasis	Marked inflammation and necrosis	Periportal fibrin deposits, hemorrhagic hepatocellular necrosis, inflammation	Centrilobular cholestasis, no inflammation	Unknown	Unknown
Treatment	Immediate delivery, supportive	Supportive	$MgSO_4$ seizure prophylaxis, delivery (delayed in very selected preterm cases), anti-hypertensive treatment	Ursodeoxycholic acid, corticosteroids, cholestyramine all of reported benefit, vitamin K	Plasma exchange, FFP infusion pending initiation of plasma exchange, corticosteroids/ antiplatelet agents	Plasma exchange, FFP infusion pending initiation of plasma exchange, corticosteroids/ antiplatelet agents

Abbreviations: DIC, disseminated intravascular coagulation; FFP, fresh frozen plasma; MgSO4, magnesium sulfate; WBC, white blood cell count.

Modified from McNulty J. Acute fatty liver of pregnancy. In: Foley MR, Strong TH, Garite TJ, editors. Obstetric intensive care manual. 2nd ed. New York (NY): McGraw-Hill; 2004. p. 212–3.

Approximately one half of patients with acute fatty liver of pregnancy will present with coexisting preeclampsia. Diagnosis of acute fatty liver of pregnancy usually is made on clinical grounds, and liver imaging or biopsy is rarely necessary. The maternal mortality rate is less than 10%. However, significant morbidity, including disseminated intravascular coagulation and acute renal failure, is present in approximately 50% of patients. The perinatal mortality rate is 10–15%, whereas the neonatal morbidity rate is high because of an increased risk of preterm delivery. Management consists of maternal stabilization and supportive care (eg, correction of coagulopathy and hypoglycemia) followed by prompt delivery. The pathogenesis of acute fatty liver of pregnancy is not well understood but some cases are associated with long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency. Fetal or placental production of long-chain fatty acids that are not cleared by the mother are toxic to the liver.

The HELLP syndrome complicates 0.5–0.9% of pregnancies and 10–20% of cases with severe preeclampsia. The typical patient presents with acute onset of malaise, nausea, vomiting, and right upper quadrant or epigastric pain. Most patients with HELLP syndrome have hypertension and proteinuria; headache is a common symptom. Patient 169 has the major laboratory abnormalities seen in this condition, which include elevated lactate dehydrogenase, microangiopathic hemolytic anemia, thrombocytopenia, and elevated liver function tests.

Both TTP and HUS are extremely rare potentially lethal microangiopathic disorders that tend to occur in the third trimester or puerperium. In patients with TTP, increased levels of large multimers of von Willebrand factor (vWF) occur secondary to markedly reduced levels of a plasma vWF-cleaving metalloprotease, which results in microvascular platelet aggregation with subsequent thrombocytopenia and microangiopathic hemolytic anemia. Large vWF multimer levels are generally not elevated in patients with HELLP syndrome. The classic pentad of TTP consists of microangiopathic hemolytic anemia, thrombocytopenia, neurologic abnormalities, renal dysfunction, and fever. Patient 170 has findings consistent with TTP.

Most cases of HUS are seen in children after *Escherichia coli* infection. Renal injury is more severe in HUS than TTP, whereas anemia and thrombocytopenia are milder. Treatment involves supportive care and daily plasmapheresis until the platelet count has normalized and hemolysis resolves. Dialysis also is required in most cases of HUS. Immediate delivery will not improve HUS or TTP.

Patient 171 has elevated transaminase levels and jaundice, normal BP, negative urine protein, and a normal platelet count, consistent with acute viral hepatitis. Hepatitis may occur in any trimester with the clinical presentation of malaise, fatigue, anorexia, nausea, abdominal pain, and jaundice. Transaminase levels may reach 1,000–2,000 units/L with hepatitis B infection, and hyperbilirubinemia occurs with variable frequency. Hepatitis serologic testing confirms the diagnosis. Pregnancy does not appear to affect the course of hepatitis B or hepatitis C infection. Similarly, hepatitis infection tends to have minimal effect on pregnancy outcome. The principal concern with hepatitis infection in pregnancy is potential transmission of the virus to the fetus. Treatment generally consists of supportive care.

Cholestasis of pregnancy typically presents in the third trimester with intractable pruritus, particularly affecting the palms and soles, and is worse at night. Elevated serum bile acids represent the classic laboratory finding. Other laboratory abnormalities may include prolonged prothrombin time and elevated transaminase and bilirubin levels. Treatment includes ursodeoxycholic acid and antihistamines for itching. Fetal well-being testing is recommended in women with cholestasis because of the increased risk of fetal heart rate tracing abnormalities and fetal demise. Delivery is recommended at or near term. Cholestasis of pregnancy usually resolves within the first few days after delivery.

Haram K, Svendsen E, Abildgaard U. The HELLP syndrome: clinical issues and management. A Review. BMC Pregnancy Childbirth 2009;9:8.

Sibai BM. Imitators of severe pre-eclampsia. Semin Perinatol 2009; 33:196–205.

Viral hepatitis in pregnancy. ACOG Practice Bulletin No. 86. American College of Obstetricians and Gynecologists. Obstet Gynecol 2007; 110:941–56.

Appendix A

Normal Values for Laboratory Tests*

Analyte	Conventional Units
Alanine aminotransferase, serum	8–35 units/L
Alkaline phosphatase, serum	15–120 units/L
Menopause	
Amniotic fluid index	3–30 mL
Amylase	20–300 units/L
Greater than 60 years old	21–160 units/L
Aspartate aminotransferase, serum	15–30 units/L
Bicarbonate	
Arterial blood	21–27 mEq/L
Venous plasma	23–29 mEq/L
Bilirubin	
Total	0.3–1 mg/dL
Conjugated (direct)	0.1–0.4 mg/dL
Newborn, total	1–10 mg/dL
Blood gases (arterial) and pulmonary function	
Base deficit	Less than 3 mEq/L
Base excess, arterial blood, calculated	–2 mEq/L to +3 mEq/L
Forced expiratory volume (FEV_1)	3.5–5 L
	Greater than 80% of predicted value
Forced vital capacity	3.5–5 L
Oxygen saturation (So_2)	95% or higher
Pao_2	80 mm Hg or more
Pco_2	35–45 mm Hg
Po_2	80–95 mm Hg
Peak expiratory flow rate	Approximately 450 L/min
pH	7.35–7.45
Pvo_2	30–40 mm Hg
Blood urea nitrogen	
Adult	7–18 mg/dL
Greater than 60 years old	8–20 mg/dL
CA 125	Less than 34 units/mL
Calcium	
Ionized	4.6–5.3 mg/dL
Serum	8.6–10 mg/dL
Chloride	98–106 mEq/L
Cholesterol	
Total	
Desirable	140–199 mg/dL
Borderline high	200–239 mg/dL
High	240 mg/dL or more
High-density lipoprotein	40–85 mg/dL
Low-density lipoprotein	
Desirable	Less than 130 mg/dL
Borderline high	140–159 mg/dL
High	Greater than 160 mg/dL
Total cholesterol-to-high-density lipoprotein ratio	
Desirable	Less than 3
Borderline high	3–5
High	Greater than 5
Triglycerides	
20 years and older	Less than 150 mg/dL
Less than 20 years old	35–135 mg/dL

*Values listed are specific for adults or women, if relevant, unless otherwise differentiated.

(continued)

Normal Values for Laboratory Tests* (*continued*)

Analyte	Conventional Units
Cortisol, plasma	
8 AM	5–23 micrograms/dL
4 PM	3–15 micrograms/dL
10 PM	Less than 50% of 8 AM value
Creatinine, serum	0.6–1.2 mg/dL
Dehydroepiandrosterone sulfate	60–340 micrograms/dL
Erythrocyte	
Count	3,800,000–5,100,000/mm^3
Distribution width	10 plus or minus 1.5%
Sedimentation rate	
Wintrobe method	0–15 mm/hour
Westergren method	0–20 mm/hour
Estradiol-17β	
Follicular phase	30–100 pg/mL
Ovulatory phase	200–400 pg/mL
Luteal phase	50–140 pg/mL
Child	0.8–56 pg/mL
Ferritin, serum	18–160 micrograms/L
Fibrinogen	150–400 mg/dL
Follicle-stimulating hormone	
Premenopause	2.8–17.2 mIU/mL
Midcycle peak	15–35 mIU/mL
Postmenopause	24–170 mIU/mL
Child	0.1–7 mIU/mL
Glucose	
Fasting	70–105 mg/dL
2-hour postprandial	Less than 120 mg/dL
Random blood	65–110 mg/dL
Hematocrit	36–48%
Hemoglobin	12–16 g/dL
Fetal	Less than 1% of total
Hemoglobin A_{1c} (nondiabetic)	5.5–8.5%
Human chorionic gonadotropin	0–5 mIU/mL
Pregnant	Greater than 5 mIU/mL
17α-Hydroxyprogesterone	
Adult	50–300 ng/dL
Child	32–63 ng/dL
25-Hydroxyvitamin D	10–55 ng/mL
International Normalized Ratio	Greater than 1
Prothrombin time	10–13 seconds
Iron, serum	65–165 micrograms/dL
Binding capacity total	240–450 micrograms/dL
Lactate dehydrogenase, serum	313–618 units/L
Leukocytes	
Total	5,000–10,000/cubic micrometers
Differential counts	
Basophils	0–1%
Eosinophils	1–3%
Lymphocytes	25–33%
Monocytes	3–7%
Myelocytes	0%
Band neutrophils	3–5%
Segmented neutrophils	54–62%

*Values listed are specific for adults or women, if relevant, unless otherwise differentiated.

(*continued*)

Normal Values for Laboratory Tests* (*continued*)

Analyte	Conventional Units
Lipase	
60 years or younger	10–140 units/L
Older than 60 years	18–180 units/L
Luteinizing hormone	
Follicular phase	3.6–29.4 mIU/mL
Midcycle peak	58–204 mIU/mL
Postmenopause	35–129 mIU/mL
Child	0.5–10.3 mIU/mL
Magnesium	
Adult	1.6–2.6 mg/dL
Child	1.7–2.1 mg/dL
Newborn	1.5–2.2 mg/dL
Mean corpuscular	
mCH Hemoglobin	27–33 pg
mCHC Hemoglobin concentration	33–37 g/dL
mCV Volume	80–100 cubic micrometers
Partial thromboplastin time, activated	21–35 seconds
Phosphate, inorganic phosphorus	2.5–4.5 mg/dL
Platelet count	140,000–400,000/mm^3
Potassium	3.5–5.3 mEq/L
Progesterone	
Follicular phase	Less than 3 ng/mL
Luteal phase	2.5–28 ng/mL
On oral contraceptives	0.1–0.3 ng/mL
Secretory phase	5–30 ng/mL
Older than 60 years	0–0.2 ng/mL
1st trimester	9–47 ng/mL
2nd trimester	16.8–146 ng/mL
3rd trimester	55–255 ng/mL
Prolactin	0–17 ng/mL
Pregnant	34–386 ng/mL by 3rd trimester
Prothrombin time	10–13 seconds
Reticulocyte count	Absolute: 25,000–85,000 cubic micrometers 0.5–2.5% of erythrocytes
Semen analysis, spermatozoa	
Antisperm antibody	% of sperm binding by immunobead technique; Greater than 20% = decreased fertility
Count	Greater than or equal to 20 million/mL
Motility	Greater than or equal to 50%
Morphology	Greater than or equal to 15% normal forms
Sodium	135–145 mEq/L
Testosterone, female	
Total	6–86 ng/dL
Pregnant	3–4 × normal
Postmenopause	½ of normal
Free	
20–29 years old	0.9–3.2 pg/mL
30–39 years old	0.8–3 pg/mL
40–49 years old	0.6–2.5 pg/mL
50–59 years old	0.3–2.7 pg/mL
Older than 60 years	0.2–2.2 pg/mL
Thyroid-stimulating hormone	0.2–3 microunits/mL
Thyroxine	
Serum free	0.9–2.3 ng/dL
Total	1.5–4.5 micrograms/dL

*Values listed are specific for adults or women, if relevant, unless otherwise differentiated.

(continued)

Normal Values for Laboratory Tests* (*continued*)

Analyte	Conventional Units
Triiodothyronine uptake	25–35%
Urea nitrogen, blood	
Adult	7–18 mg/dL
Older than 60 years	8–20 mg/dL
Uric acid, serum	2.6–6 mg/dL
Urinalysis	
Epithelial cells	0–3/HPF
Erythrocytes	0–3/HPF
Leukocytes	0–4/HPF
Protein (albumin)	
Qualitative	None detected
Quantitative	10–100 mg/24 hours
Pregnancy	Less than 300 mg/24 hours
Urine specific gravity	
Normal hydration and volume	1.005–1.03
Concentrated	1.025–1.03
Diluted	1.001–1.01

*Values listed are specific for adults or women, if relevant, unless otherwise differentiated.

Appendix B

Laboratory and Clinical Criteria for the Diagnosis of Antiphospholipid Syndrome

Laboratory Criteria

- Lupus anticoagulant present in plasma, on two or more occasions at least 12 weeks apart. It is interpreted as either present or absent. Testing for lupus anticoagulant is ideally performed before the patient is treated with anticoagulants, or
- Anticardiolipin antibody of immunoglobulin G isotype or immunoglobulin M isotype in serum or plasma, or both, present in medium or high titer (ie, greater than 40 GPL or MPL, or greater than the 99th percentile), on two or more occasions, at least 12 weeks apart, or
- Anti-β_2-glycoprotein I of immunoglobulin G isotype or immunoglobulin M isotype in serum or plasma (in titer greater than 99th percentile for abnormal population as defined by the laboratory performing the test), or both, present on two or more occasions, at least 12 weeks apart.

Clinical Criteria

- Vascular thrombosis
- One or more clinical episodes of arterial, venous, or small vessel thrombosis, in any tissue or organ, or
- Pregnancy morbidity
  - — One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation, with normal fetal morphology documented by ultrasonography or by direct examination of the fetus, or
  - — One or more premature births of a morphologically normal neonate before the 34th week of gestation because of eclampsia or severe preeclampsia, or features consistent with placental insufficiency, or
  - — Three or more unexplained consecutive spontaneous pregnancy losses before the 10th week of pregnancy, with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded.

Modified from Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295–306.

Appendix C

Risk Factors for Preterm Birth

History

- Obstetric–gynecologic history: prior spontaneous preterm birth (spontaneous preterm birth of twins is not a significant risk factor when the next pregnancy is a singleton pregnancy); prior second-trimester loss; two or more prior dilation and evacuations; prior cone biopsy; uterine anomalies; diethylstilbestrol exposure; myomata; extremes of interpregnancy interval; assisted reproductive technology
- Maternal lifestyle (eg, smoking, drug abuse, sexually transmitted infections)
- Maternal prepregnancy weight less than 50 kg (120 lb) or low body mass index (weight in kilograms divided by height in meters squared [kg/m^2] less than 18.5); poor nutritional status
- Maternal age (younger than 19 years; 35 years or older)
- Race (especially African American)
- Education (less than 12th grade)
- Certain medical conditions (eg, diabetes mellitus, hypertension)
- Low socioeconomic status
- Limited prenatal care
- Family history of spontaneous preterm birth (poorly studied)
- Vaginal bleeding (especially during second trimester)
- Stress (mostly related to above risks)

Identifiable by screening

- Anemia
- Periodontal disease
- Cervical length less than 25 mm on transvaginal ultrasonography (especially before 30 weeks of gestation)
- Positive fetal fibronectin test result (greater than 50 ng/mL between 22 weeks and 34 weeks of gestation)

Usually symptomatic

- Uterine contractions

Indicated preterm birth

- Abruptio placentae
- Fetal demise/major anomaly/compromise/hydramnios
- Placenta previa
- Major maternal disease (eg, hypertensive complications, diabetes mellitus)

Appendix D

Atypical Antibodies and the Relationship to Fetal Hemolytic Disease

Blood Group System	Antigens Related to Hemolytic Disease	Hemolytic Disease Severity	Proposed Management
Lewis	*		
I	*		
Kell	K	Mild to severe†	Fetal assessment
	k	Mild	Routine obstetric care
	Ko	Mild	Routine obstetric care
	Kp^a	Mild	Routine obstetric care
	Kp^b	Mild	Routine obstetric care
	Js^a	Mild	Routine obstetric care
	Js^b	Mild	Routine obstetric care
Rh (non-D)	E	Mild to severe†	Fetal assessment
	C	Mild to severe†	Fetal assessment
	C	Mild to severe†	Fetal assessment
Duffy	Fy^a	Mild to severe†	Fetal assessment
	Fy^b	‡	Routine obstetric care
	By^3	Mild	Routine obstetric care
Kidd	Jk^a	Mild to severe	Fetal assessment
	Jk^b	Mild	Routine obstetric care
	Jk^3	Mild	Routine obstetric care
MNSs	M	Mild to severe	Fetal assessment
	N	Mild	Routine obstetric care
	S	Mild to severe	Fetal assessment
	s	Mild to severe	Fetal assessment
	U	Mild to severe	Fetal assessment
	Mi^a	Moderate	Fetal assessment
MSSs	Mt^a	Moderate	Fetal assessment
	Vw	Mild	Routine obstetric care
	Mur	Mild	Routine obstetric care
	Hil	Mild	Routine obstetric care
	Hut	Mild	Routine obstetric care
Lutheran	Lu^a	Mild	Routine obstetric care
	Lu^b	Mild	Routine obstetric care
Diego	$D1^a$	Mild to severe	Fetal assessment
	Di^b	Mild to severe	Fetal assessment
Xg	Xg^a	Mild	Routine obstetric care
P	PP_{1pk} (Tj^a)	Mild to severe	Fetal assessment
Public antigens	Yt^a	Moderate to severe	Fetal assessment
	Yt^b	Mild	Routine obstetric care
	Lan	Mild	Routine obstetric care
	En^a	Moderate	Fetal assessment
	Ge	Mild	Routine obstetric care
	Jr^a	Mild	Routine obstetric care
	Co^a	Severe	Fetal assessment
	Co^{1-b-}	Mild	Routine obstetric care
Private antigens	Batty	Mild	Routine obstetric care
	Becker	Mild	Routine obstetric care
	Berrens	Mild	Routine obstetric care
	Biles	Moderate	Fetal assessment
	Evans	Mild	Routine obstetric care
	Gonzales	Mild	Routine obstetric care
	Good	Severe	Fetal assessment
	Heibel	Moderate	Fetal assessment

(continued)

Atypical Antibodies and the Relationship to Fetal Hemolytic Disease (*continued*)

Blood Group System	Antigens Related to Hemolytic Disease	Hemolytic Disease Severity	Proposed Management
Private antigens *(continued)*	Hunt	Mild	Routine obstetric care
	Jobbins	Mild	Routine obstetric care
	Radin	Moderate	Fetal assessment
	Rm	Mild	Routine obstetric care
	Ven	Mild	Routine obstetric care
	Wright[a]	Severe	Fetal assessment
	Wright[b]	Mild	Routine obstetric care
	Zd	Moderate	Fetal assessment

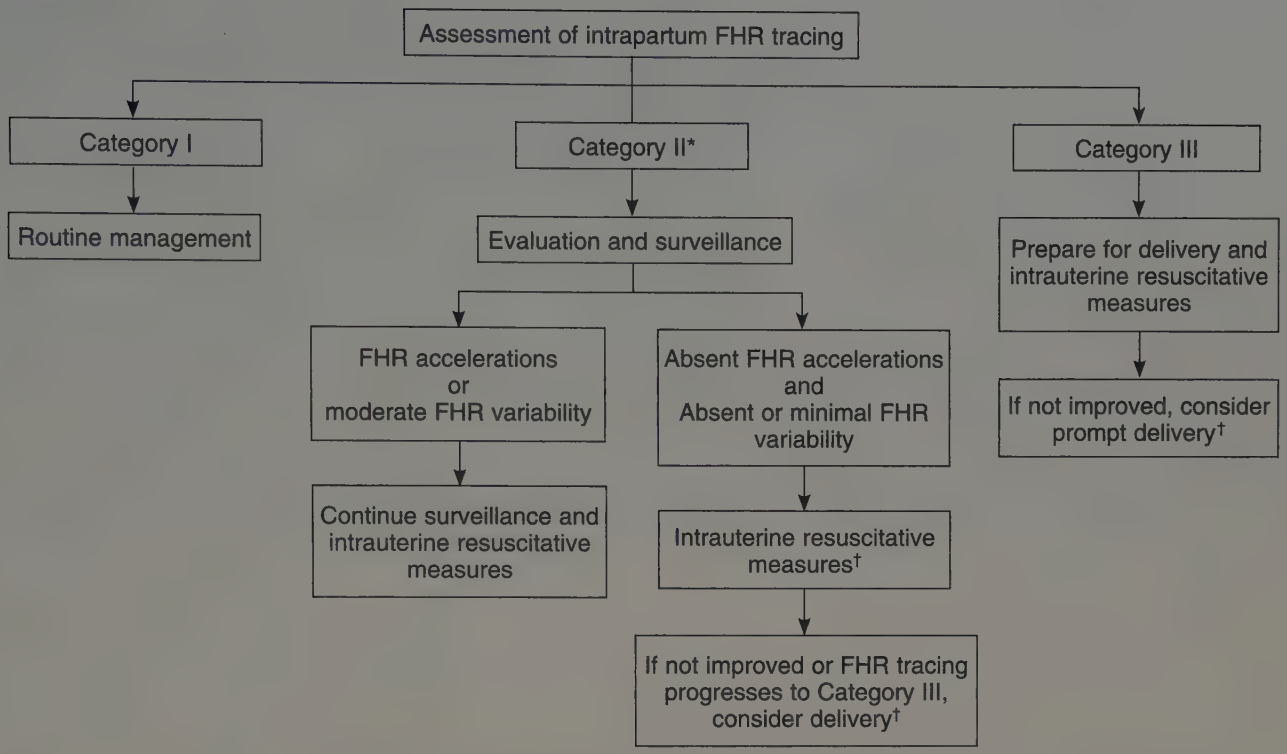
*Not a proven cause of hemolytic disease of the newborn

†With hydrops fetalis

‡Not a cause of hemolytic disease of the newborn

Adapted from Weinstein L. Irregular antibodies causing hemolytic disease of the newborn: a continuing problem. Clin Obstet Gynecol 1982;25:321.

Appendix E-1


Assessment of intrapartum FHR tracing
Category I
Routine management
Category II*
Evaluation and surveillance
FHR accelerations or moderate FHR variability
Continue surveillance and intrauterine resuscitative measures
Absent FHR accelerations and Absent or minimal FHR variability
Intrauterine resuscitative measures†
If not improved or FHR tracing progresses to Category III, consider delivery†
Category III
Prepare for delivery and intrauterine resuscitative measures
If not improved, consider prompt delivery†

*Given the wide variation of FHR tracings in Category II, this algorithm is not meant to represent assessment and management of all potential FHR tracings, but provide an action template for common clinical situations.

†Timing and mode of delivery based on feasibility and maternal–fetal status.

Fig. E-1. Management algorithm of intrapartum fetal heart rate tracings based on three-tiered category system. Abbreviation: FHR, fetal heart rate.

Appendix E-2

Various Intrauterine Resuscitative Measures for Category II or Category III Tracings or Both

Goal	Associated Fetal Heart Rate Abnormality*	Potential Intervention(s)†
Promote fetal oxygenation and improve uteroplacental blood flow	Recurrent late decelerations	Initiate lateral positioning (either left or right)
	Prolonged decelerations or bradycardia	Administer maternal oxygen administration
	Minimal or absent fetal heart rate variability	Administer intravenous fluid bolus
		Reduce uterine contraction frequency
Reduce uterine activity	Tachysystole with Category II or III tracing	Discontinue oxytocin or cervical ripening agents
		Administer tocolytic medication (eg, terbutaline)
Alleviate umbilical cord compression	Recurrent variable decelerations	Initiate maternal repositioning
	Prolonged decelerations or bradycardia	Initiate amnioinfusion
		If prolapsed umbilical cord is noted, elevate the presenting fetal part while preparations are underway for operative delivery

*Evaluation for the underlying suspected cause(s) is also an important step in management of abnormal FHR tracings.

†Depending on the suspected underlying cause(s) of FHR abnormality, combining multiple interventions simultaneously may be appropriate and potentially more effective than doing individually or serially (Simpson KR, James DC. Efficacy of intrauterine resuscitation techniques in improving fetal oxygen status during labor. Obstet Gynecol 2005;105:1362–8).

Data from Young BK, Katz M, Klein SA, Silverman F. Fetal blood and tissue pH with moderate bradycardia. Am J Obstet Gynecol 1979;135:45–7; Chauhan SP, Roach H, Naef RW 2nd, Magann EF, Morrison JC, Martin JN Jr. Cesarean section for suspected fetal distress. Does the decision-incision time make a difference? J Reprod Med 1997;42:347–52; Schauberger CW, Chauhan SP. Emergency cesarean section and the 30-minute rule: definitions. Am J Perinatol 2009;26:221–6; *and* Schifrin BS, Hamilton-Rubinstein T, Shields JR. Fetal heart rate patterns and the timing of fetal injury. J Perinatol 1994;14:174–81.

Appendix F

Inclusion Criteria, Treatment Regimens, and Outcomes of Large Randomized Control Trials of Magnesium Neuroprotection and Cerebral Palsy

Author	No.	Inclusion Criteria	Magnesium Sulfate Treatment Protocol	Death and CP RR (95% CI)	CP RR (95% CI)
Crowther (2003)	1, 255	GA <30 weeks Likely PTB <24 hours	4-g load, 1 g/hour	0.83 (0.66–1.03)	0.83 (0.54–1.27)
Marret (2007)	688	GA <33 weeks	4-g load only	0.80 (0.58–1.1)	0.70 (0.41–1.19)
Rouse (2008)	2,241	GA 24–31 weeks High risk of PTB	6-g load, 2 g/hour	0.97 (0.77–1.23)	0.55 (0.32–0.95)

Abbreviations: CI, confidence interval; CP, cerebral palsy; GA, gestational age; PTB, preterm birth; RR, relative risk;.

Data from Crowther CA, Hiller JE, Doyle LW, Haslam RR; Australasian Collaborative Trial of Magnesium Sulphate (ACTOMg SO4) Collaborative Group. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. JAMA 2003;290:2669–76; Marret S, Marpeau L, Zupan-Simunek V, Eurin D, Lévêque C, Hellot MF, et al. Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial. PREMAG trial group. BJOG 2007;114:310–8; *and* Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. Eunice Kennedy Shriver NICHD Maternal–Fetal Medicine Units Network. N Engl J Med 2008;359:895–905.

Appendix G

Various Tocolytic Agents by Dosage, Administration, Contraindications, and Maternal and Fetal–Neonatal Side Effects

Tocolytic Agent	Dosage and Administration	Contraindications	Maternal Side Effects	Fetal–Neonatal Side Effects
Beta-mimetic	Terbutaline .25 mg subcutaneous every 20 minutes to 3 hours (hold for pulse greater than 120 bpm)	Cardiac arrhythmias	Cardiac or cardiopulmonary arrhythmias, pulmonary edema, myocardial ischemia, hypotension, tachycardia	Fetal tachycardia, hyperinsulinemia, hyper glycemia, myocardial and septal hypertrophy ischemia
		Poorly controlled thyroid disease	Metabolic hyperglycemia, hyperinsulinemia, hypokalemia, antidiuresis, altered thyroid function	Neonatal tachycardia, hypoglycemia, hypocalcemia, hyperbili-rubinemia, hypotension, intraventricular hemorrhage
		Poorly controlled diabetes mellitus	Physiologic tremor, palpitations, nervousness, nausea, vomiting, fever, hallucinations	
Magnesium sulfate	4.0–6.0 g bolus for 20 minutes, then 4–6 g per hour	Myasthenia gravis	Flushing, lethargy, headache, muscle weakness, nausea, vomiting, fever, hallucinations	Lethargy, hypotonia, respiratory depression, demineralization with prolonged use
Calcium channel blockers	30 mg loading dose, then 10–20 mg every 4–6 hours	Cardiac disease Use with caution with renal disease	Flushing, headache, dizziness, nausea, transient hypotension	None noted as yet
		Maternal hypotension (less than 90/50 mm Hg)		
		Avoid concomitant use with magnesium sulfate		
Prostaglandin synthetase inhibitors	Indomethacin loading dose of 50 mg rectally or 50–100 mg orally, then 25–50 mg orally every 4 hours for 48 hours	Significant renal or hepatic impairment	Nausea, heartburn	Constriction of ductus arteriosus, pulmonary hypertension, reversible decrease in renal function with oligohydramnios, intraventricular hemorrhage, hyperbilirubinemia, necrotizing enterocolitis
	Ketorolac loading dose of 60 mg intramuscularly, then 30 mg intramuscularly every 6 hours for 48 hours	Active peptic ulcer		
	Sulindac 200 mg orally every 12 hours for 48 hours	Coagulation disorders or thrombocytopenia		
		NSAIDs-sensitive asthma		
		Other sensitivity to NSAIDs		

Abbreviations: bpm, beats per minute; NSAIDs, nonsteroidal antiinflammatory drugs.

Hearne AE, Nagey DA. Therapeutic agents in preterm labor: tocolytic agents. Clin Obstet Gynecol 2000;43:787–801. Copyright 2000 by Elsevier.

Index

A
Abdomen, acute, 88
ABO blood group, 26
Abortifacient, methotrexate as, 16
Abortion, recurrent spontaneous, 97
Abscess(es), perispinal, 1
Accelerated starvation of pregnancy, 121
Acidemia
  mixed, 152–154
  respiratory, 152–154
Acute abdomen, in pregnancy, 88
Acute chest syndrome, sickle cell disease and, 111
Acute fatty liver of pregnancy, 72, 168–171
Acute viral hepatitis, acute fatty liver of pregnancy versus, 168–171
Acyclovir, for herpes simplex virus infection in pregnancy, 27
S-Adenosyl-L-methionine, for intrahepatic cholestasis of pregnancy, 75
β-Adrenergic blockers, in migraine prevention, 127
Age
  as factor in breast cancer, 79
  gestational, 21, 60
β_2-Agonists, inhaled, 160–163
Air travel, 63
Alcohol use, in pregnancy, 93
Allergy, penicillin, 44
Alloimmunization
  detection of, 76
  Kell, 76
  maternal, 76
Alpha-fetoprotein, pregnancy effects of, 28
American College of Medical Genetics, on cystic fibrosis screening, 125
American College of Obstetricians and Gynecologists
  on antenatal corticosteroids for fetal neuroprotection, 122
  on asthma medications during pregnancy, 61
  on cesarean delivery, 14
  on cystic fibrosis screening, 125
  on estimating delivery date based on ultrasonography, 103
  on fetal alcohol syndrome and fetal alcohol spectrum disorders prevention, 93
  on gestational diabetes screening, 35
  on human immunodeficiency virus screening during pregnancy, 83
  on magnesium sulfate for fetal neuroprotection, 122, 130
  on prophylactic antibiotic administration for cesarean delivery, 104
  on screening for intimate partner death, 115
  on vanity (keepsake) ultrasonography, 68
American College of Rheumatology, on systemic lupus erythematosus, 52
American Diabetes Association, on gestational diabetes screening, 35
American Institute of Ultrasound in Medicine, on vanity (keepsake) ultrasonography, 68
American Pregnancy Association, on hemolysis, elevated liver enzymes, and low platelet count syndrome, 95
American Society of Reproductive Medicine, on pregnancy in human immunodeficiency virus patients, 45
Amniocentesis
  for cytomegalovirus DNA polymerase chain reaction, 32
  in fetal anemia detection, 76
Amnioinfusion, 100
Amniotic fluid embolus, 109
Amniotic fluid index, in oligohydramnios evaluation, 56
Anaphylactoid syndrome of pregnancy, 109
Anastomotic leaks, in bariatric surgery patients, 59
Anemia, 74
  defined, 33, 74
  fetal, 76
  iron-deficiency, 74
  microcytic, 33
  sickle cell, 111
  workup for, 33
Anesthesia and anesthetics
  complications of, 70
  epidural, 1, 64. *See also* Epidural anesthesia
  obesity effects on, 11
  regional, 64
Aneuploidy screening, 135–138
Angiotensin-converting enzyme inhibitors
  in heart failure, 39
  maternal and fetal effects of, 9
  during pregnancy, 34
Anti-D immune globulin, non-RhD alloimmunized pregnancies related to, 76
Antibiotic(s)
  for asymptomatic bacteriuria, 96
  in cesarean delivery, 104
  for chorioamnionitis, 129
  for community-acquired pneumonia, 25
  in preterm premature rupture of membranes management, 24
Antibodies, RhD, 76
Anticoagulant(s)
  for antiphospholipid syndrome, 19
  for pulmonary embolism, 67
Anticoagulation, peripartum, 99
Anticonvulsive syndromes, fetal, 102
Antidepressant(s), in migraine prevention, 127
Antiepileptic drug(s), for seizures, 102
Antiepileptic drug syndromes, 102
Antihypertensive(s), maternal and fetal effects of, 9
Antiphospholipid syndrome, 19, 97
Antiretroviral therapy, in mother-to-child human immunodeficiency virus transmission prevention, 112
Antithrombin III deficiency, 113
Antiviral therapy, for genital herpes in patients with preterm premature rupture of membranes, 42
Appendicitis, 86, 88
Arthritis, rheumatoid, 52
Ashkenazi Jewish descent
  cystic fibrosis in people of, 125
  genetic screening for women of, 58
Aspiration, during anesthesia administration, 70
Assisted reproductive technology, human immunodeficiency virus-related, 45
Asthma
  control of, 160–163
  environmental triggers in, 160–163
  peak expiratory flow rate in, 160–163
  peak flow meter in, 160–163
  in pregnancy, 160–163
  severity classification for, 61, 160–163
  treatment of, 61, 160–163
Autoimmune disorders, pregnancy and, 52
Autonomy, in medical decision making, 60
Azithromycin, for community-acquired pneumonia, 25

B
Bacille Calmette-Guérin vaccine, in tuberculosis prevention, 54
Bacterial endocarditis, subacute, 90
Bacterial pneumonia, aspiration-induced lung injury and, 70
Bacterial vaginosis, 96
Bacteriuria, asymptomatic, 96
Balloon catheter, for postpartum hemorrhage, 31
Bariatric surgery patients, complications in, 59
Beneficence, in medical decision making, 60
Beta-mimetics, for tocolysis, 164–167
Betamethasone, in pregnancy, 5, 42
Biophysical profile, in pregnancy management, 120
Biophysical profile scoring, 120
Birth. *See also* Preterm birth
β-Blockers, in heart failure, 39
Blood, O-negative, 26
B-Lynch suture, for postpartum hemorrhage, 31
Bone mass index, as factor in cesarean delivery, 11
Bowel obstruction, in bariatric surgery patients, 59
Breast cancer
  in pregnancy, 79
  prevalence of, 79
Breast mass, in pregnancy, 79
Breastfeeding
  importance of, 66
  prevalence of, 66
Breech presentation, prevalence of, 128
Bromocriptine mesylate, in peripartum cardiomyopathy, 39
Bupropion, sustained-release, during pregnancy, 87

C
Calcium channel blockers
  in migraine prevention, 127
  for tocolysis, 149–151, 164–167
Cancer, breast, 79
Cardiac afterload, during pregnancy, 124
Cardiac disease, pregnant women with, 124
Cardiac output, during labor, 124
Cardiomyopathy, peripartum, 39, 81
Cardiovascular physiology, 124
Carpal tunnel syndrome, 52
Category III fetal heart rate tracing, 71

CDC. *See* Centers for Disease Control and Prevention
Centers for Disease Control and Prevention (CDC)
on fetal alcohol syndrome, 93
on group B streptococci prevention, 44
on herpes C virus screening in pregnancy, 94
on human immunodeficiency virus screening in pregnancy, 83, 112
on herpes simplex virus, 27
on human papillomavirus vaccine in pregnancy, 139–143
on intimate partner death, 115
on intimate partner violence, 115
on postpartum contraception, 15
on syphilis management, 2
on syphilis screening, 2
Cephalosporins, in cesarean delivery, 104
Cerclage, in preterm birth prevention, 119
Cerebral palsy, 122, 130
Cervical insufficiency, 96
Cervical length, 110, 117
Cervicovaginal secretions, fetal fibronectin in, 117
Cervix, shortened, 117
Cesarean delivery
antibiotic administration timing for, 104
body mass index and, 11
elective, 14
herpes simplex virus infection and, 27
macrosomia and, 3, 114
prevalence of, 14
prior T-shaped incision, 114
regional anesthesia during, 64
transverse, 128
vaginal birth after, 98
wound disruption related to, 11
Chorioamnionitis, cerebral palsy related to, 122
Cholestasis, fetal risks associated with, 75
Cholestasis of pregnancy, acute fatty liver of pregnancy versus, 168–171
Chorioamnionitis, 1, 88, 129
causes of, 129
defined, 129
diagnosis of, 129
treatment of, 129
Chorionicity, in twin pregnancies management, 91
Chronic hypertension, in pregnancy, 84
Circle of Willis, 76
Clindamycin
in group B streptococci prevention, 44
for mastitis, 66
Cluster headache, 73
CMV. *See* Cytomegalovirus
Coagulopathy(ies)
dilutional, 95
disseminated intravascular, 95
Cocaine use, in pregnancy, 18
Codeine, in migraine prevention, 127
Community-acquired pneumonia, 25
Congenital cytomegalovirus, in pregnancy, 126
Congenital malformations, methotrexate and, 16
Contraception, postpartum, 15
Contraceptives
long-acting reversible, 77
oral, 15
Contraction(s), during labor, 105
Control of Hypertension in Pregnancy Study, 84
Corticosteroid(s)
for asthma, 61
for fetal neuroprotection, 122
for nausea and vomiting in pregnancy, 108
in pregnancy, 5
in preterm premature rupture of membranes management, 24
Cyclooxygenase inhibitors, for tocolysis, 164–167
Cystic fibrosis, 125
Cystitis, 88
Cytomegalovirus (CMV)
congenital, 126
fetal, 32
in pregnancy, 32, 126

D

Death, fetal, 69, 123
Deep venous thrombosis inherited thrombophilia in patient with, 113
Delicatessen meat, listeriosis due to, 13
Delivery. *See also* Cesarean delivery; Vaginal delivery
forceps, 7
by obese patient, 11
preterm, 110
Depression
intimate partner violence related to, 115
in pregnancy, 23
screening for, 23
Dexamethasone, in pregnancy, 5
Diabetes mellitus, 121
gestational. *See* Gestational diabetes mellitus
type, 1, 116
Dicloxacillin, for mastitis, 66
Diet, in gestational diabetes mellitus management, 41
Dilutional coagulopathy, 95
Diphtheria and reduced tetanus toxoids and acellular pertussis vaccine, in pregnancy, 139–143
Disseminated intravascular coagulation, 95
Disseminated intravascular coagulopathy, 95
Diuretics
in heart failure, 39
for peripartum cardiomyopathy, 81
Doppler ultrasonography
in fetal anemia detection, 76
in intrauterine growth restriction, 62
in placenta accreta detection, 106
Down syndrome
antenatal detection of, 30
ultrasonographic markers of, 30
Doxylamine succinate, for nausea and vomiting in pregnancy, 108
Drug exposure, during pregnancy, 34
Dumping syndrome, in bariatric surgery patients, 59
Dysautonomia, familial, 58
Dystocia
labor, 10
shoulder, 65, 92

E

Echogenic bowel, cystic fibrosis and, 125
Ectopic pregnancies, methotrexate in, 16
Edinburgh Postnatal Depression Scale, 23
Electronic fetal heart rate monitoring, 100, 144–148
ELISA. *See* Enzyme-linked immunosorbent assay
Embolism, pulmonary, 67
Embolus, amniotic fluid, 109
Embryo, malformation of, 4
Emergency Medical Treatment and Active Labor Act, 55, 71
End-stage renal disease, pregnancy in women with, 33
Endocarditis, subacute bacterial, 90
Environment, as factor in asthma, 160–163
Enzyme-linked immunosorbent assay (ELISA)
in hepatitis C virus screening in pregnancy, 94
in human immunodeficiency virus screening in labor, 112
in syphilis screening, 2
Epidural anesthesia
chorioamnionitis and, 1
complications of, 1, 64
fever related to, 64
Epilepsy, described, 102
Erythromycin
for mastitis, 66
in preterm premature rupture of membranes management, 24
Erythropoietin
for anemia, 74
during pregnancy in women with end-stage renal disease, 33
Ethical issues
in medical dilemma, 60
patient transfer–related, 71
Ethnicity, in gestational diabetes mellitus, 51
Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network study, 130
Exercise, in gestational diabetes mellitus management, 41
External cephalic version, 128

F

Factor V Leiden mutation, 40, 113
False labor, contractions in, 105
Familial dysautonomia, 58
FAS. *See* Fetal alcohol syndrome
FASDs. *See* Fetal alcohol spectrum disorders
Fatty acids, omega-3, 107
Ferric gluconate, for anemia, 74
Fetal acid–base assessment, 152–154
Fetal acid–base status, fetal heart rate variability effects on, 152–154
Fetal alcohol spectrum disorders (FASDs), 93
Fetal alcohol syndrome (FAS), 93
Fetal anemia, detection of, 76
Fetal anticonvulsive syndromes, 102
Fetal blood sampling, in fetal anemia detection, 76
Fetal cytomegalovirus, diagnosis of, 32
Fetal death, 69, 123
trial of labor after cesarean delivery for, 123
vaginal delivery for, 123
Fetal fibronectin, in cervicovaginal secretions, 117
Fetal heart rate (FHR)
decelerations, epidural anesthesia and, 64
monitoring, electronic, 100, 144–148
variability, in fetal acid–base status, 152–154
Fetal hyperthyroidism, 48
Fetal lung maturity testing, 17
Fetal movement
assessment of, 36
decreased, 36

NOTE: Numbers refer to questions, not pages.

Fetal neuroprotection
antenatal corticosteroids for, 122
magnesium sulfate for, 122, 130
Fetus, cholestasis effects on, 75
Fever
epidural anesthesia and, 64
postpartum, 80
FHR. *See* Fetal heart rate
Fibroadenomas, 79
Fish consumption, in pregnancy, 107
Folate, for anemia, 74
Foley catheter, transcervical, 123
Folic acid, in periconception period, 4
Folic acid supplementation, in reproductive-aged women, 16
Fondaparinux sodium
for pulmonary embolism, 67
for thrombophilia, 40
Food and Drug Administration
on mercury levels in salmon, 107
on smoking cessation, 87
on terbutaline in pregnancy, 149–151
on vanity (keepsake) ultrasonography, 68
Forceps delivery, 7
Free thyroxine, in pregnancy, 116
Furosemide, for peripartum cardiomyopathy, 39

G

G20210A gene mutation, 113
Galactoceles, 79
Gaskin maneuver, in shoulder dystocia management, 92
Gastric bypass surgery, in obese parturient, 59
GBS. *See* Group B streptococci
Genetic screening, in women of Ashkenazi Jewish descent, 58
Genital herpes
in patient with preterm premature rupture of membranes, 42
suppressive therapy for, 27
Gestational age, 21, 60
Gestational diabetes mellitus, 34, 35
defined, 35
ethnicity in, 51
pathophysiology of, 51
prevalence of, 51
prevention of, 51
recurrence of, 51
risk factors for, 51
screening for, 35
treatment of, 41
Gestational thrombocytopenia, 38
Ginger, in nausea and vomiting prevention, 108
50-g Glucose challenge tests, in gestational diabetes mellitus screening, 35
Glucose intolerance, in pregnancy, 41
Glucose metabolism, in pregnancy, 121
50-g Glucose tolerance test, in gestational diabetes mellitus recurrence assessment, 51
Glyburide, in gestational diabetes mellitus management, 41
Graves disease, fetal hyperthyroidism and, 48
Group B streptococci (GBS)
penicillin allergy and, 44
treatment of, 44

H

Hashimoto disease, 116
Headache(s). *See also* Migraine; *specific types*
causes of, *73*
in pregnancy, *73*
Healthy People 2020 Goal, for breastfeeding, 66
Heart failure, peripartum cardiomyopathy and, 39
Hematoma, vulvar, 12
Hemoglobin A, disorders related to, 155–159
Hemoglobin Bart, 155–159
Hemoglobin S, sickle cell disease due to, 155–159
Hemoglobinopathy(ies), 155–159
Hemolysis, elevated liver enzymes, and low platelet count syndrome, 72, 78, 168–171
clinical course of, 78
defined, 95
differential diagnosis of, 78
laboratory tests for, 78
maternal death due to, 78
preeclampsia, acute fatty liver of pregnancy versus, 168–171
prevalence of, 78
treatment of, 78
Hemolytic disease, of the newborn, 76
Hemolytic uremic syndrome, 72, 168–171
Hemorrhage, postpartum, 26, 31
Heparin
low molecular weight, 99
for pulmonary embolism, 67
for thrombophilia, 40
unfractionated, 99
Heparin-induced thrombocytopenia, 67
Hepatitis, acute viral, 168–171
Hepatitis A virus vaccine, 139–143
Hepatitis B virus, 131–134
Hepatitis C virus, screening in pregnancy, 94
Herpes simplex virus, infection, 27
Centers for Disease Control and Prevention on, 27
management of, 27
in neonates, 27
in patient with preterm premature rupture of membranes, 42
in pregnancy, 27
HITS questionnaire, 115
HIV. See Human immunodeficiency virus
Hospital transfers, Emergency Medical Treatment and Active Labor Act on, 55
Human chorionic gonadotropin, synthesis of, 28
Human immunodeficiency virus (HIV), 45
in labor patient, 112
in pregnancy, 45, 83
screening during pregnancy, 83, 112
thrombocytopenia and, 8
transmission prevention of, 112
Human papillomavirus vaccine, in pregnancy, 139–143
Human placental lactogen, glucose elevation due to, 121
Huntington procedure, for uterine inversion, 29
Hydramnios, evaluation of, 101
17-α-Hydroxyprogesterone caproate
in cervical length maintenance, 110
in recurrent preterm delivery prevention, 119
Hyperemesis gravidarum, 108
Hypertension
chronic, 84
during pregnancy, 34, 84
pulmonary, 111
Hyperthyroidism
fetal, 48
maternal, 48
Hypoglycemic agents, for gestational diabetes mellitus, 41
Hypokalemia, terbutaline for, 164–167
Hypotension
epidural anesthesia and, 64
nifedipine for, 164–167
Hypothyroidism, 116
Hypoxemia, maternal, 109
Hysterectomy, for postpartum hemorrhage, 31
Hysteroscopic sterilization, in pregnancy prevention, 77

I

Illicit drug use, in reproductive-aged women, 18
Immune thrombocytopenic purpura, 38
Immunization(s)
influenza, 57
in pregnancy, 139–143
immunoglobulin G testing
for parvovirus, 53
for toxoplasmosis, 43
Immunoglobulin M testing
for parvovirus, 53
for toxoplasmosis, 43
Indomethacin,
adverse effects of, 149–151
for oligohydramnios, 149–151, 164–167
for tocolysis, 149–151
Induction of labor, 82, 118
indications for, 118
with transcervical Foley catheter, 123
Influenza
individuals at risk of complications of, 57
transmission of, 57
vaccination for, 57
Influenza vaccine, 139–143
Inhaled β_2-agonists, for asthma, 160–163
Inhaled corticosteroids, for asthma, 61
Inherited thrombophilia, 113
Inhibin A, pregnancy effects of, 28
Insulin, for gestational diabetes mellitus, 41
International Federation of Gynecology and Obstetrics, on cesarean delivery, 14
International Headache Society, on migraine, 73
Intimate partner violence, 115
Intrahepatic cholestasis of pregnancy, 20, 37, 75
defined, 37
mild, 37
Intrapartum electronic fetal monitoring, nomenclature related to, 144–148
Intrauterine devices, in pregnancy prevention, 77
Intrauterine growth restriction (IUGR), 62
Intravenous ferric gluconate, for anemia, 74
Iodine deficiency, hypothyroidism due to, 116
Iron-deficiency anemia, 74
Iron supplementation, for anemia, 33, 74
IUGR. *See* Intrauterine growth restriction

J

Justice, in medical decision making, 60

K

Karyotype(s), abnormal, 69
Keepsake ultrasonography, 68
Kell alloimmunization, 76
Kleihauer-Betke test, in placental abruption diagnosis, 6

NOTE: Numbers refer to questions, not pages.

L
Labor
beginning, 105
cardiac output during, 124
contractions in, 105
duration of, 10
human immunodeficiency virus in patient in, 112
induction of, 82, 118, 123
latent phase of, 105
normal, 10
preterm, 96
rapid enzyme-linked immunosorbent assay testing in, 112
Labor dystocia, 10
Lactational mastitis, 66
Lambda sign, 85
Laparoscopic sterilization, in pregnancy prevention, 77
Laparotomy, for uterine inversion, 29
Learning deficits, mercury and, 107
Legal issues, patient transfer, 71
Levetiracetam, for seizures, 102
Levonorgestrel intrauterine device, in pregnancy prevention, 77
Levonorgestrel-releasing intrauterine system, in pregnancy prevention, 77
Levosimendan, in peripartum cardiomyopathy, 39
Lifestyle changes, in migraine prevention, 127
Listeria monocytogenes, 13
Listeriosis, 13
Live attenuated influenza virus vaccine, 57
Long-acting reversible contraceptives, in pregnancy prevention, 77
Lung injury, aspiration-induced, 70

M
Macrosomia, 3, 114
Magnesium sulfate
in cerebral palsy prevention, 122
contraindications to, 149–151
in fetal neuroprotection, 130
in myasthenia gravis, 149–151, 164–167
for tocolysis, 149–151
toxicity of, 109
Magnetic resonance imaging, in placenta accreta detection, 106
Mammography, in breast cancer detection, 79
Mantoux skin test, contraindications to, 54
Mastitis, 66, 79
lactational, 66
methicillin-resistant *Staphylococcus aureus* and, 66
treatment of, 66
Maternal alloimmunization, 76
Maternal death, hemolysis, elevated liver enzymes, and low platelet count syndrome and, 78
Maternal hyperthyroidism, 48
Maternal hypothyroidism, 116
Maternal hypoxemia, amniotic fluid embolus and, 109
McRoberts maneuver, 65, 92
MDR3 (ABCB4) gene, in intrahepatic cholestasis of pregnancy, 37
Measles, mumps, and rubella vaccine, in pregnancy, 139–143
Medical decision making, autonomy in, 60
Medical dilemmas, ethical issues in, 60
Memory deficits, mercury and, 107
Mendelson syndrome, 70
Meningitis, epidural anesthesia and, 1
Mercury, childhood learning and memory deficits related to, 107
Metformin, in gestational diabetes mellitus management, 41
Methamphetamine, in pregnancy, 18
Methicillin-resistant *Staphylococcus aureus*, mastitis and, 66
Methotrexate
congenital malformations due to, 16
uses of, 16
15-Methyl prostaglandin $F_{2\alpha}$, for postpartum hemorrhage, 31
Methylene tetrahydrofolate reductase mutation, 113
Methylmercury, childhood learning and memory deficits related to, 107
Microcytic anemia, thalassemia in, 33
Migraine, 127
diagnosis of, 73
management of, 127
in pregnancy, 73
prevention of, 127
Mild intrahepatic cholestasis of pregnancy, 37
Misoprostol, for postpartum hemorrhage, 31
Mitral regurgitation, 90
Mitral stenosis, in pregnancy, 124
Mitral valve prolapse, 90
Mixed acidemia, 152–154
Monochorionic twins, 91
Motor vehicle collision, 50
Multiple sclerosis, 89
Multivitamin, in nausea and vomiting prevention, 108
Myasthenia gravis, magnesium sulfate in, 149–151, 164–167
Mycobacterium tuberculosis, 54

N
National Health and Nutritional Examination Survey, on herpes simplex virus, 27
National Heart, Lung, and Blood Institute, on asthma control, 160–163
National HIV/AIDS Clinicians' Consultation Center, on human immunodeficiency virus screening during pregnancy, 83
National Institute of Child Health and Human Development, workshop on electronic fetal monitoring of, 144–148
National Institutes of Health
on asthma medications during pregnancy, 61
on cesarean delivery, 14
National Institute of Child Health and Human Development workshop on electronic fetal monitoring of, 144–148
on screening for glucose intolerance in pregnancy, 41
Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure of, 84
National Violent Death Reporting System, on intimate partner death, 115
Nausea and vomiting, in pregnancy, 108
Neonatal resuscitation, hospital standards for, 55
Neonate(s), herpes simplex virus in, 27
Neural tube defects, prevention of, 4
Nicotine replacement therapy, during pregnancy, 87
Nifedipine
for hypotension, 164–167
in recurrent migraine prevention, 127
for tocolysis, 149–151
Nitroglycerin, in uterine inversion management, 29
Nonmaleficence, in medical decision making, 60
Nonsteroidal antiinflammatory drugs, in pregnancy, 111
Nutritional deficits, in bariatric surgery patients, 59

O
Obesity
anesthetic complications related to, 11
delivery-related effects of, 11
gastric bypass surgery complications related to, 59
in pregnancy, 11
prenatal risks and complications associated with, 59
in reproductive-aged women, 11
venous thromboembolism related to, 11
Oligohydramnios, 56, 149–151, 164–167
Omega-3 fatty acids, in fish, 107
Ondansetron hydrochloride, for nausea and vomiting in pregnancy, 108
O-negative blood, 26
Oocyst(s), 43
Operative vaginal delivery, 7
Oral contraceptives, postpartum, 15
Osteoarthritis, 52

P
Pain relief, epidural anesthesia and, 64
PAPP-A. *See* Pregnancy-associated plasma protein-A
Parvovirus, 53
Patient transfer, legal and ethical obligations in, 71
Peak expiratory flow rate, in asthma, 160–163
Peak flow meter, in asthma, 160–163
PEFR. *See* Peak expiratory flow rate
Penicillin(s), penicillinase-resistant, 66
Penicillin allergy, group B streptococci and, 44
Penicillin G, for syphilis, 2
Penicillinase-resistant penicillins, for mastitis, 66
Periconception period, folic acid in, 4
Periodontal disease, in pregnancy, 49
Perinatal survival, 21
Peripartum anticoagulation, 99
Peripartum cardiomyopathy, 39, 81
Perispinal abscess, epidural anesthesia and, 1
Periviable birth, 60
Permanent sterilization, in pregnancy prevention, 77
Phenylephrine, for sinus headache, 127
Physical violence, defined, 115
Placenta accreta, diagnosis of, 106
Placenta previa
described, 106
at 20 weeks gestation, 106
Placental abruption, 6
Pneumonia(s)
bacterial, 70
causes of, 25
community-acquired, 25
influenza, 57
Polymerase chain reaction test, in syphilis screening, 2

NOTE: Numbers refer to questions, not pages.

Positive antibody screen, 26
Postpartum contraception, Centers for Disease Control and Prevention, recommendations for, 15
Postpartum fever, 80
Postpartum hemorrhage, 26, 31
Preeclampsia, 8
  imitators of, 72
  pregnancy-associated thrombocytopenia related to, 38
Preeclampsia–eclampsia, imitators of, 72
Pregnancy
  accelerated starvation of, 121
  acute abdomen in, 88
  acute fatty liver of, 72, 168–171
  alcohol use in, 93
  anaphylactoid syndrome of, 109
  angiotensin-converting enzyme inhibitors during, 34
  appendicitis in, 86
  asthma in, 160–163
  asthma medications during, 61
  autoimmune disorders and, 52
  biophysical profile in management of, 120
  breast cancer in, 79
  breast mass during, 79
  cardiac afterload during, 124
  cardiac disease during, 124
  cardiovascular physiology in, 124
  cholestasis of, 168–171
  chorioamnionitis in, 1
  chronic hypertension in, 84
  cocaine use in, 18
  congenital cytomegalovirus in, 126
  cytomegalovirus in, 32
  dating of, 103
  depression in, 23
  diabetes mellitus during, 34
  disseminated intravascular coagulopathy in, 95
  drug exposure during, 34
  ectopic, 16
  fish consumption during, 107
  glucose metabolism changes during, 121
  headache in, 73
  hemodynamic changes of, 124
  hepatitis C virus screening in, 94
  human immunodeficiency virus during, 45
  human immunodeficiency virus screening during, 83
  hypertension during, 34, 84
  intrahepatic cholestasis of, 20, 37, 75
  listeriosis prevention in, 13
  methamphetamine in, 18
  migraine in, 73
  mitral stenosis in, 124
  multiple sclerosis in, 89
  nausea and vomiting in, 108
  nonsteroidal antiinflammatory drugs in, 111
  obesity in, 11
  periodontal disease in, 49
  prevention of, 77
  radiation exposure during, 63
  Rh disease in, 76
  RhD antibodies in, 76
  seat belt use in, 50
  serum markers effects on, 28
  smoking during, 87
  statins during, 34
  steroid use in, 5
  thrombosis during, 63
Pregnancy *(continued)*
  thyroid replacement requirements during, 116
  thyroid testing during, 116
  toxoplasmosis in, 43
  vaccinations in, 53, 139–143
  venous thromboembolism in, 15
  vibroacoustic stimulation in, 22
Pregnancy-associated plasma protein-A (PAPP-A), 28
Pregnancy loss
  recurrent, 97
  thrombophilias and, 97
  uterine anomalies and, 96
Premature infants, respiratory distress syndrome in, 17
Premature rupture of membranes, preterm, 24, 42
Preterm birth
  air travel and, 63
  causes of, 96
  cerebral palsy related to, 122
  cervical length effects on, 110, 117
  defined, 96, 119
  factors affecting, 46, 47
  infant morbidity and mortality related to, 119
  neonatal mortality associated with, 149–151
  prevalence of, 164–167
  prevention of, 119
  recurrent, 119
  shortened cervix and, 117
  smoking cessation in prevention of, 46, 47
Preterm labor, defined, 96
Preterm premature rupture of membranes; 24, 42
Prior T-shaped incision cesarean delivery, trial of labor after cesarean delivery, contraindication due to, 114
Proctoepisiotomy, in shoulder dystocia management, 92
Progesterone
  in cervical length maintenance, 110
  in reducing risk of preterm birth, 117
Propranolol, in migraine prevention, 127
Prostaglandin synthetase inhibitors, for tocolysis, 149–151
Protamine sulfate, in anticoagulation in pregnancy, 99
Prozone phenomenon, 2
Pruritus, epidural anesthesia and, 64
Psychological and emotional violence, 115
Pulmonary embolism, 67
Pulmonary hypertension, sickle cell disease and, 111
Pyelonephritis, 1, 88

Q

Quintero staging system, 85

R

Radiation exposure, during pregnancy, 63
Rapid enzyme-linked immunosorbent assay testing in labor, 112
Reactive nonstress test result, defined, 22
Recurrent pregnancy loss, 97
Recurrent preterm delivery, prevention of, 119
Recurrent spontaneous abortion, 97
Regional anesthesia
  case-fatality rate associated with, 64
  complications related to, 64
Respiratory acidemia, 152–154
Respiratory arrest, in healthy parturient, 109
Respiratory distress syndrome, in premature infants, 17
Respiratory failure, aspiration and, 70
Resuscitation, neonatal, 55
RhD antibodies, in pregnancy, 76
Rhesus disease, in pregnancy, 76
Rheumatoid arthritis, 52
Rh-negative patient, 26
Rho (D) immune globulin, in Rh-negative pregnant women involved in motor vehicle collision, 50
Rubin maneuver, in shoulder dystocia management, 92
Rupture of membranes, preterm premature, 24, 42

S

Salmon, mercury level in, 107
Seat belt use, in pregnancy, 50
Seizure disorder, medications for, 102
Sepsis, sickle cell disease and, 111
Serum markers, adverse pregnancy outcome related to, 28
Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, of National Institutes of Health, 84
Sexual intercourse, preterm birth related to, 119
Sexual violence, 115
Shoulder dystocia, 65, 92
Sickle β-thalassemia, hemoglobin in, 155–159
Sickle cell anemia, maternal complications of, 111
Sickle cell disease, 111, hemoglobin in, 155–159
Sickle cell trait, hemoglobin in, 155–159
Simvastatin, during pregnancy, 34
Single deepest pocket technique, in oligohydramnios evaluation, 56
Sinus headache, phenylephrine for, 127
Sjögren syndrome, 52
SLE. *See* Systemic lupus erythematosus
Smead–Jones mass closure, 11
Smoking, during pregnancy, 87
Smoking cessation, 87
  agents in, 87
  in migraine prevention, 127
  in preterm birth prevention, 46, 47
Society for Maternal–Fetal Medicine, on magnesium sulfate for fetal neuroprotection, 130
Society of Obstetricians and Gynaecologists of Canada, on cesarean delivery, 14
Spontaneous abortion, recurrent, 97
Staphylococcus aureus, methicillin-resistant, 66
Statin(s), during pregnancy, 34
Sterilization, methods for, 77
Steroid(s)
  for hemolysis, elevated liver enzymes, and low platelet count syndrome, 78
  in pregnancy, 5
Stillbirth, 69
Subacute bacterial endocarditis, 90
Syncytiotrophoblast(s), in human chorionic gonadotropin synthesis, 28
Syphilis, 2
Systemic lupus erythematosus (SLE), 52, 72
  symptoms of, 72
  thrombocytopenia and, 38
Systolic/diastolic ratio, in intrauterine growth restriction, 62

NOTE: Numbers refer to questions, not pages.

T

T-ACE Problem Drinking Screen, 93
TB. *See* Tuberculosis
Tension headache, 73
Teratogenesis, antiepileptic drugs and, 102
Terbutaline
  for hypokalemia, 164–167
  for tocolysis, 149–151
Term gestation, confirmation of, 118
Thalassemia, in microcytic anemia, 33
  α-Thalassemia, hemoglobin in, 155–159
  β-Thalassemia, hemoglobin in, 155–159
Thrombocytopenia, 8, 38
  causes of, 8
  classification of, 8
  defined, 8, 38
  diagnosis of, 8
  differential diagnosis of, 8
  dilutional coagulopathy and, 95
  gestational, 38
  heparin-induced, 67
  types of, 38
Thromboembolic disease, sickle cell disease and, 111
Thromboembolism, venous, 11, 15
Thrombophilia
  inherited, 113
  management of, 40
Thrombophilia(s), first-trimester pregnancy loss and, 97
Thrombosis, during pregnancy, 63
Thrombotic thrombocytopenic purpura, 72, 168–172
Thyroid disease, in reproductive-age women, 48
Thyroid replacement requirements, during pregnancy, 116
Thyroid-stimulating hormone, in pregnancy, 116
Thyroid testing, during pregnancy, 116
Tocolysis
  contraindications to, 164–167
  maternal and fetal adverse effects of, 149–151
Tocolytic therapy
  after preterm premature rupture of membranes, 24
  in prolonging pregnancy, 122
TOLAC. *See* Trial of labor after cesarean delivery
Tooth loss, maternal, 49
Toxoplasma gondii, in pregnancy, 43
Toxoplasmosis, in pregnancy, 43
Transcervical Foley balloon, for trial of labor after cesarean delivery candidates, 82
Transcervical Foley catheter, labor induction with, 123
Transient fetal heart rate decelerations, epidural anesthesia and, 64
Transverse cesarean delivery, external cephalic version following, 128
Travel, air, 63
Treponema pallidum, syphilis due to, 2
Trial of labor after cesarean delivery (TOLAC), 82, 98
  candidates for, 114
  contraindication to, 114
  fetal death and, 123
  guidelines for, 114
Triplets, management of, 46
Trivalent inactivation virus vaccine, 57
True labor, contractions in, 105
"T" sign at membrane insertion, in monochorionic pregnancy diagnosis, 91
Tubal sterilization, 77
Tuberculin skin testing, 54
Tuberculosis (TB), 54
Twin(s), monochorionic, 91
Twin peak sign, 85
Twin pregnancies, chorionicity in management of, 91
Twin–twin transfusion syndrome, 85

U

Ultrasonographic markers, in Down syndrome, 30
Ultrasonography
  in angiotensin-converting enzyme inhibitors-associated fetal abnormalities identification, 9
  in appendicitis diagnosis, 86
  for breast mass in pregnancy, 79
  in cytomegalovirus, 32
  in cystic fibrosis, 125
  Doppler. *See* Doppler ultrasonography
  in pregnancy dating, 103
  vanity (keepsake), 68
Umbilical cord blood gas measurement, in assessing fetal acid–based status immediately before birth, 152–154
Unconjugated estriol, pregnancy effects of, 28
Unfractionated heparin, in anticoagulation in pregnancy, 99
Urinary tract infections, upper versus lower, 88
Ursodeoxycholic acid, for intrahepatic cholestasis of pregnancy, 20, 75
U.S. Preventive Services Task Force, in syphilis screening, 2
U.S. Public Health Service, on management of human immunodeficiency virus patient in labor, 112
Uterine anomalies, preterm birth and pregnancy loss associated with, 96
Uterine artery embolization, for postpartum hemorrhage, 31
Uterine artery ligation, for postpartum hemorrhage, 31
Uterine inversion, 29
Uterine packing, for postpartum hemorrhage, 31
Uterotonic agents, for postpartum hemorrhage, 31

V

Vaccination(s)
  influenza, 57
  in pregnancy, 139–143
Vaccine(s)
  Bacille Calmette-Guérin, 54
  diphtheria and reduced tetanus toxoids and acellular pertussis vaccine, 139–143
  hepatitis A, 139–143
  influenza, 139–143
  live attenuated influenza virus, 57
  measles, mumps, and rubella, 139–143
  in pregnancy, 139–143
  trivalent inactivation virus, 57
  varicella, 139–143
Vacuum delivery, 7
Vaginal delivery
  after cesarean delivery, 98, 114
  fetal death and, 123
  operative, 7
Vaginal progesterone
  in cervical length maintenance, 110
  in preterm birth prevention, 117, 119
Vaginosis, bacterial, 96
Valproate, for seizures, 102
Vanity (keepsake) ultrasonography, 68
Varenicline, during pregnancy, 87
Varicella vaccine, in pregnancy, 139–143
Vasectomy, in pregnancy prevention, 77
Venereal Disease Research Laboratory test, in syphilis screening, 2
Venous thromboembolism
  obesity and, 11
  in pregnancy, 15
Vibroacoustic stimulation, in pregnancy, 22
Violence
  intimate partner, 115
  types of, 115
Vitamin B_6, for nausea and vomiting in pregnancy, 108
Vomiting, in pregnancy, 108
Vulvar hematoma, 12

W

Warfarin sodium
  for pulmonary embolism, 67
  for thrombophilia, 40
Western blot test, in human immunodeficiency virus screening in labor, 112
Woods corkscrew, in shoulder dystocia management, 92
Wound disruption, cesarean deliveries and, 11

Z

Zavanelli maneuver, in shoulder dystocia management, 92

NOTE: Numbers refer to questions, not pages.

FIG. 2-1. Syphilitic chancre of the vulva. (Image copyright Science Photo Library.)

Fig. 6-1. Example of a Couvelaire uterus. (Courtesy of Keith Nelson, MD.)

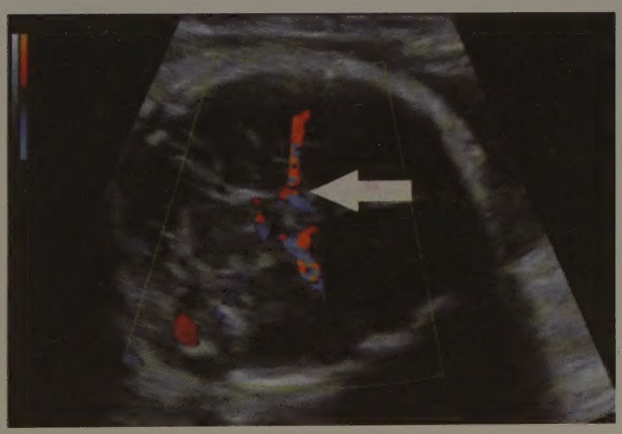


Fig. 76-1. Middle cerebral artery Doppler using color flow to locate the vessel. Arrow notes the proper location for the pulsed Doppler gate on the middle cerebral artery vessel closest to the transducer. (Moise KJ. Management of rhesus alloimmunization in pregnancy. Obstet Gynecol 2008;112:164–76.)

COUNTWAY LIBRARY
3 2044 132 078 304

COUNTWAY LIBRARY
3 2044 132 078 304

ISBN 978-1-934984-22-2
17500 >
EAN
9 781934 984222